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# Editorial

## A Re-evaluation of the Indications for Cardiac Fluoroscopy*

New standards of medical x-ray protection have been prepared by the National Committee on Radiation Protection reducing the maximum permissible radiation dose.[1] The Committee has also advised that current methods and procedures should be reviewed to determine whether satisfactory results could be obtained with less radiation than is now generally employed. It has been stated[2] that "no (radiation) exposure level that is capable of reduction should be considered a safe level." In view of these recommendations, we have re-examined the status of fluoroscopy in cardiac diagnosis. As the standard fluoroscopic examination of the heart exposes patients to as much as one thousand times the radiation they would receive in taking the standard PA and lateral chest x-ray examination, it is obvious that the use of the latter procedures is preferable whenever it might give the same diagnostic information.

It has been demonstrated[3] that the fluoroscope under the best of conditions emits about 4 roentgens/min while the *average* fluoroscope in the clinician's office emits 15 roentgens/min. During the average fluoroscopic examination of the heart and chest, the clinician exposes the patient for up to two and one-half minutes, giving the patient a total exposure of from 10 r. to 37 r. In taking the standard PA and lateral chest x-ray, however, the average exposure is only 0.002 r. The National Bureau of Standards has stated[1] that the maximum permissible dose to patients under 18 years of age should be not more than 1.5 r. per year. For patients between the ages of 18 to 45 years and for workers in radiology, at any age, the maximum permissible total weekly dose should be not more than 0.3 r., or an annual dose of 5 r. It is obvious that in routine cardiac fluoroscopy, this maximum permissible dose may be readily exceeded.

The dangers to the patient of exposure to ionizing rays are both gonadal and somatic. Recent studies have suggested that when the gonads are exposed to radiation, mutations of offspring and even temporary sterilization may result. If the x-ray tube and fluoroscopic screen are well shielded, the exposure to the gonads will be essentially that of scattered radiation. The radiation hazards of a somatic nature are the possible induction of malignancies such as leukemia, depression of the bone marrow, depilation, ulceration and dermatitis.

*Precautions to Be Taken by the Fluoroscopist:* When the cardiologist performs a fluoroscopic examination, he should be shielded with leaded apron and gloves and the exposed part of the face, neck, and shoulders protected behind the leaded fluoroscopic screen. The protective apron

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and gloves should be checked for leaks from time to time to insure that no primary radiation will strike the fluoroscopist. Scattered radiation which bounces off the patient or the walls of the room may reach considerable proportions, particularly if a defect in the protective mechanisms of the x-ray apparatus has occurred. Scott has stated that the scattered radiation hazard to the fluoroscopist is greatest when fluoroscopy is conducted on the table in the transverse plane.[4] The fluoroscopist should conduct the examination with the lowest radiation output possible, in the shortest time, in the upright position with the fluoroscopic screen shuttered to the maximum degree. The fluoroscopist's eyes should be dark-adapted for at least 10 minutes in order to shorten the time of exposure and keep the radiation dosage below 6.0 r. per min.

*Re-evaluation of Indications for Chest Fluoroscopy:* Knowing that the patient and the fluoroscopist should be exposed to as little radiation as possible, we must re-examine the indications for cardiac fluoroscopy and ask ourselves if there are other ways of obtaining the same information with less radiation exposure. Warren[5] has recommended, "If each physician would ask himself before ordering a diagnostic procedure, 'is this really necessary,' much unnecessary radiation could be avoided." Many radiologists have recommended that the "routine" cardiac fluoroscopy be abandoned and that this procedure be utilized only if the PA and lateral chest films reveal some cardiac abnormality that requires further investigation. Many have stated that the PA and lateral x-ray examination of the chest will reveal most of the cardiac abnormalities that may be found on fluoroscopy. The exposure to the patient is one thousand times less than that of routine fluoroscopic examination. On the other hand, many cardiologists enjoy studying the motion of the heart and state that fluoroscopy gives them a better understanding of the patient's problems.

Actually, there is little to be learned from the motion of the heart that cannot be observed from the routine chest film except paradoxical pulsations due to ventricular aneurysms, movements of the diaphragm and the hilar dance. Unless the fluoroscopist becomes very expert in visualizing the movements of the ventricle, he may be unable to ascertain whether there is a paradoxical pulsation except by prolonged visualization of the systolic contraction. The roentgenkymogram which graphically photographs the degree and direction of movement of the heart may be used to demonstrate ventricular aneurysms with comparatively little roentgen exposure. The electrocardiogram also often aids in the diagnosis of ventricular aneurysm. "Fluoroscopy is of value in determining the amplitude of pulsation of the pulmonary artery and its major branches; however, the conventional chest roentgenogram will usually reveal such enlargement of these structures as to indicate clearly that a shunt is present. In the differential diagnosis of post-stenotic dilation of the pulmonary artery and primary pulmonary hypertension, it also may be of some importance."[6]

Fluoroscopic examination for aneurysm of the aorta requires a great deal of radiation exposure because the movements of the mediastinum are difficult to visualize. The roentgenkymogram will demonstrate an aneurysm of the aorta with much less exposure and more certainty. Calcification of the valves can often be demonstrated by special x-ray technics requiring far less radiation exposure than fluoroscopy. The barium swallow is used routinely to demonstrate fluoroscopically an encroachment of the atrium on the esophagus by an enlarged left atrium. Radiologists may also obtain this information with a barium swallow using the right anterior oblique roentgenogram. Chamber enlargement may be ascertained from routine PA, lateral and oblique chest films as efficiently as with cardiac fluoroscopy. Electrocardiograms may demonstrate chamber enlargements more accurately than radiological methods.

Chest films give a permanent record of the heart and reveal most cardiac abnormalities. These film records may be compared from time to time, an important advantage which is not afforded by fluoroscopy. The cardiologist, using simple procedures such as auscultation, the electrocardiogram, chest radiography, roentgenkymography, circulation times, and venous pressure determination may amass sufficient information so that the need for fluoroscopy will be limited. The use of the fluoroscope in cardiologic practice should be reserved for further

investigation of abnormalities detected in the routine chest film or clinical examination. By using the fluoroscope or the image intensifier fluoroscope[7] only when abnormalities require definitive investigation, the cardiologist and the patient will receive a minimum amount of radiation exposure. The image intensifier should be used especially by cardiac catheterization personnel who are at present being exposed to radiation in excess of the permissible dose.

The future offers many advances in diagnostic procedures such as image cineroentgenography.[8] This new technic which is now nearly perfected can be used to study movements of the heart with a minimum amount of radiation exposure. The cardiologist is able to view the same record over and over without exposure and may project it against a screen for greater magnification. It will probably offer a great amount of information for diagnostic purposes with minimum radiation exposure.

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# Clinical Studies

# The Syndrome of Ventricular Septal Defect With Aortic Insufficiency*

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THE SYNDROME of congenital ventricular septal defect with aortic insufficiency, due to unsupported or deformed aortic valve cusps, has been infrequently reported in the medical literature.[1–28]

During the past four years we have had the opportunity to observe seven patients we believe to be examples of this entity.

At times the clinical diagnosis is relatively easy but usually further diagnostic studies are necessary for confirmation. The correct diagnosis is of considerable importance since certain of these patients, including two of our own, have been thought erroneously to have a patent ductus arteriosus.[9,10,18,21,23,24,25,27]

The usual auscultatory findings in ventricular septal defect complicated by aortic insufficiency are a loud systolic murmur heard maximally in the left 2nd to 4th interspaces and a high-pitched aortic diastolic murmur transmitted down the left sternal border. The murmur in some instances may be continuous.[3,9,10,13,15,19,25,26] A wide pulse pressure and the peripheral signs of aortic insufficiency are present.

The purpose of this report is to present seven cases of this anomaly, to review previously reported cases, to discuss the differential diagnosis, and to suggest the methods whereby a correct diagnosis may be made.

## CASE HISTORIES

CASE 1. P.C., a 17-year-old white girl, was known to have a heart murmur since her first year of life. From childhood her physical growth and development had been retarded and she had been aware of decreased exercise tolerance and thoracic deformity. She allegedly had rheumatic fever when six years of age. In 1949 an attempt at surgical correction of the kyphoscoliosis was made without success. In 1951 she developed congestive failure requiring digitalis and diuretics. On September 9, 1953, she was admitted to the hospital for diagnostic evaluation and treatment.

*Physical examination* revealed a physically underdeveloped but mentally alert young female, comfortable at rest in a semi-Fowler's position but dyspneic on slight activity. Her weight was 86 pounds. The blood pressure was 134/44. There was marked kyphoscoliosis of the dorsal spine to the right with asymmetry of the chest, the left side being prominent. The heart was markedly enlarged, the apex being in the left mid-axillary line. Auricular fibrillation was present. A systolic thrill was palpable along the left sternal margin. There was a loud harsh systolic murmur over the entire precordium, but loudest in the 2nd left interspace. Also heard maximally in the 2nd left interspace was a loud blowing diastolic murmur. Evidences of congestive failure included distended neck veins, rales in both lower lung fields, edema of the lower extremities, and prolonged circulation time.

*Roentgenograms* revealed marked cardiac enlargement, a prominent pulmonary artery and pulmonary overcirculation (Fig. 1). An electrocardiogram revealed auricular fibrillation and combined ventricular hypertrophy.

On salt restriction and diuretic therapy she lost six

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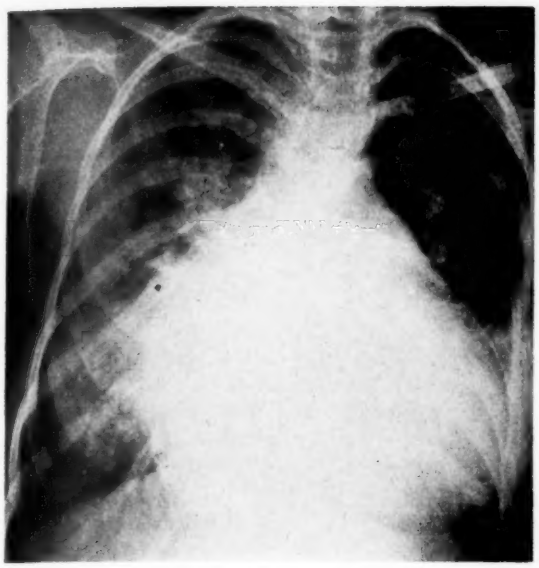


Fig. 1. Case 1. PA teleo of chest (9-9-53) showing dextroscoliosis of the spine, small aortic knob, moderately prominent pulmonary artery segment, greatly increased transverse diameter of the heart and overcirculation of the lungs.

pounds and improved considerably. While the patient was under optimal control, cardiac catheterization was performed. The results were as follows:

| | *$O_2$ content vol. %* | *Pressure mm Hg* |
|---|---|---|
| Superior vena cava | 8.6 | 6/3 |
| Right atrium | 8.9 | 8/4 |
| Right ventricle (inflow) | 9.5 | 90/4 |
| Left pulmonary artery | 14.3 | 90/55 |
| Right pulmonary artery | 13.7 | 90/55 |
| Brachial artery | 17.9 (96% saturated) | 142/24 |
| Systemic flow | 3.3 *l*/min | |
| Cardiac index | 2.6 *l*/min/M² | |
| Pulmonary flow | 7.5 *l*/min | |
| Left-to-right shunt | 4.2 *l*/min | |
| Total pulmonary resistance | 787 dynes sec $cm^{-5}$ | |
| Area of defect | 1.6 $cm^2$ | |

With the demonstration of a left to right shunt and a high arterial pulse pressure the cardiac lesion was diagnosed as patent ductus arteriosus. Surgical therapy was considered but because of the poor risk, was not advised.

*Clinical Course:* She was returned home and did fairly well until February 1954, when the congestive failure became more difficult to control. In spite of repeated injections of mercurial diuretics, increasing edema, nausea, vomiting, and respiratory distress developed.

On re-admission to the hospital on March 16, 1954, she appeared acutely ill with hyperventilation, venous distention, and edema which was more marked in the right leg. An electrocardiogram suggested digitalis intoxication with frequent ventricular premature contractions. The blood count was unremarkable. Urinalysis showed 3 plus albuminuria. Digitalis was discontinued. She improved slowly but the edema in her right leg persisted. Later the right saphenous vein became palpable and hard, and anticoagulant therapy was instituted.

On April 9 she developed intermittent fever rising to 100.8° F. It was noted that the hemoglobin had fallen from 14.8 g to 10.9 g and the sedimentation rate had risen from 8 to 42 mm per hour. The spleen was palpated by one observer. Seven blood cultures and two urine cultures revealed no growth.

A presumptive diagnosis of subacute bacterial endocarditis was made and she was given 5 million units of penicillin and one gram of streptomycin a day, but this was discontinued after a week. The congestive failure was finally controlled with digitalis, rigid salt restriction and Diamox.

She was discharged and returned weekly for outpatient care. Congestive failure recurred at home and she was readmitted to the hospital. Neither Diamox nor mercurial diuretics resulted in diuresis.

The course was steadily downhill and she expired in congestive heart failure on July 30, 1954.

*Autopsy:* The important findings were localized to the cardiovascular system. The transverse diameter of the thorax was 24 cm and the transverse diameter of the heart was 17 cm. The entire lateral margin of the heart was in contact with the lateral thoracic wall, the cardiac apex being in the 7th intercostal space. The right pleural cavity contained 700 cc and the left 500 cc of dark brown, thin fluid. The entire left lung showed a marked degree of atelectasis.

The heart was markedly enlarged, weighing 530 g. Both ventricles were dilated. The trabeculae carneae and papillary musculature of the right ventricle were considerably thicker than those of the left ventricle. The right ventricle averaged 7 mm and the left, 12 mm in

Fig. 2. Case 1. Autopsy specimen of heart viewed from the left ventricular side. Note the crescent-shaped ventricular septal defect located just beneath the noncoronary aortic valve cusp and subtracting from its support.

thickness. The circumferences of the valves in millimeters were as follows: pulmonary, 80; aortic, 63; tricuspid, 145; mitral, 110. The membranous portion of the interventricular septum revealed a crescent-shaped defect 1.4 cm in diameter (Fig. 2). This defect was located just below the noncoronary aortic cusp, subtracting from its support and causing it to be displaced slightly below the superior margin of the right and left aortic cusps. It was obvious on inspection that the three aortic valve cusps could not be approximated and that this resulted in insufficiency of the aortic valve. The edge of the defect was made up of a thick ridge of very dense fibrous tissue. From the left ventricular side the

Fig. 3. Case 1. Ventricular septal defect as viewed from the right ventricular side. The noncoronary aortic valve cusp can be seen through the defect.

septal cusp of the tricuspid valve could be visualized through the defect. On the right ventricular side the defect in the membranous septum was roughly circular in shape and 2 cm in diameter (Fig. 3). On the lateral wall of the right ventricle, in a direct line with the ventricular septal defect, was a triangular area of thickened endocardium 1.8 cm in greatest width. The remainder of the endocardium was not remarkable. The walls of the coronary arteries were soft and their intimal surfaces were smooth.

The right lung weighed 500 g and was very edematous; the lower lobe contained a markedly increased amount of blood. The left lung weighed 350 g and was partially atelectatic and subcrepitant. The spleen was small, weighing 80 g. The liver was congested and weighed 900 g. The remainder of the gross examination was essentially unremarkable except for congestive changes.

Microscopic examination of the heart showed no appreciable increase in interstitial connective tissue. The large and small arteries were essentially normal. Microscopic examination of the lungs revealed moderate and occasionally marked medial hypertrophy of the small arteries. The arterioles were similarly involved.

*Final Diagnosis:* The final significant anatomic diagnoses were:

(1) Large defect of membranous interventricular septum with loss of septal support of noncoronary aortic valve cusp with insufficiency of aortic valve.

(2) Myocardial hypertrophy involving both ventricles, more marked in the right.

(3) Local endocardial fibrosis of the right ventricle (at the point of impact of the shunted blood).

(4) Sclerosis of the small pulmonary arteries and arterioles.

(5) Chronic passive congestion of viscera.

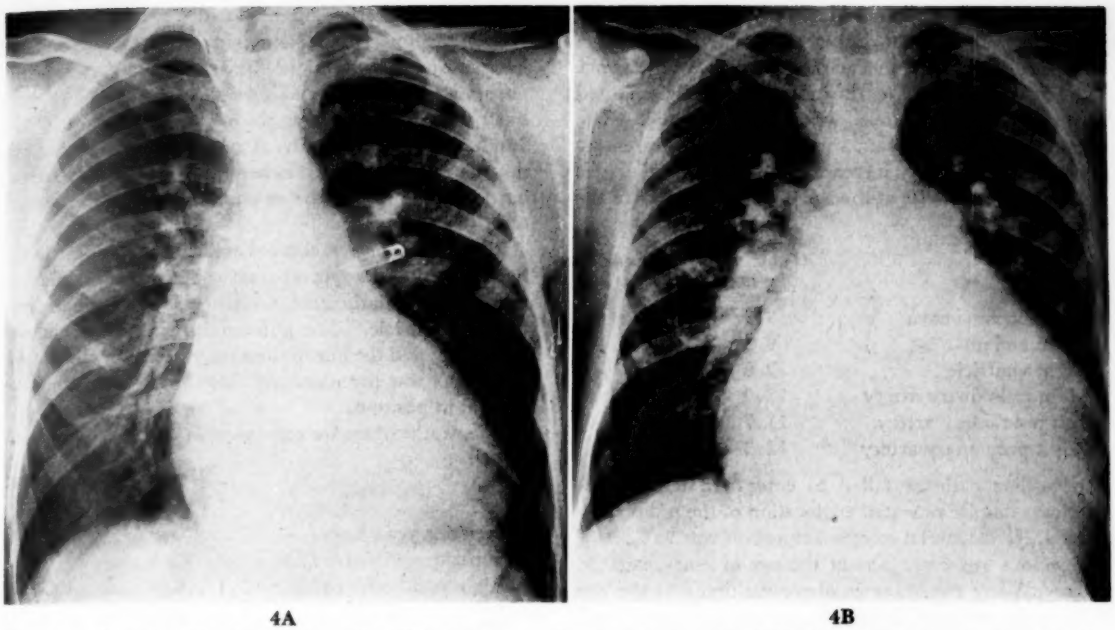
(6) Bilateral hydrothorax, ascites, and peripheral edema.

(7) Kyphoscoliosis of dorsal spine.

Case 2. P. K., a 17-year-old white male, was known to have had heart disease since infancy. At the age of nine years he developed staphylococcal subacute bacterial endocarditis which responded to penicillin therapy. Recurrent epistaxis occurred from the age of six years, requiring repeated electrical cauterization of the right side of the nasal septum. Diminished exercise tolerance was noted for the first time at the age of 13 years and was associated with progressive cardiac enlargement (Fig. 4A). About one year later a prolonged episode of paroxysmal auricular tachycardia occurred and was controlled with digitalis therapy. Since that time he continued to take this drug which was later supplemented with quinidine sulfate. At the age of 15, congestive failure supervened (Fig. 4B) and the patient was given intramuscular mercurial diuretics and a low-salt diet. Two additional episodes of congestive heart failure occurred between the ages of 15 and 17 years. At no time was there evidence of cyanosis or clubbing of the digits.

*Physical Examination:* Throughout the period of observation the physical signs remained essentially unchanged. At the age of 17 his height was 68 inches and his weight 113 pounds. The abnormal physical signs were localized to the cardiovascular system. The jugular venous pressure was increased to 4 cm above the sternal angle. All the peripheral pulses were bounding with arterial Corrigan pulsations in the neck, waterhammer radial pulses, pistol shots over the femoral arteries and capillary pulsations in the nail beds. The blood pressure in the upper extremities was 130/0 and in the lower extremities 140/0. The heart was greatly enlarged with an apical left ventricular impulse in the 6th left intercostal space in the mid-axillary line. A coarse systolic thrill was palpable maximally in the 4th and 5th left parasternal spaces and radiated somewhat up the left sternal border and towards the apex. The 1st heart sound was obscured by a harsh grade IV pansystolic murmur which was maximal over the back between the scapulae. The 2nd heart sound was normally split. A grade III blowing pandiastolic murmur was audible maximally in the second right and left parasternal spaces and radiated down the left sternal border and to the apex. The liver edge was palpable 4 cm below the right costal margin. Pretibial edema and rales at both lung bases were present intermittently.

*The electrocardiogram* showed notched P waves, left axis deviation and marked left ventricular hypertrophy as well as evidence of right ventricular and septal hyper-



4A 4B

Fig. 4A. Case 2. PA teleo of chest (1-5-53) showing moderate enlargement of the heart in the transverse diameter chiefly to the left and downward, mild overcirculation of the lungs, small aortic knob and normal pulmonary artery segment with fairly large right and left main branches.

Fig. 4B. Case 2. PA teleo of chest (7-13-55) showing enormous increase in all heart dimensions. Moderate enlargement of the main pulmonary artery and its branches and overcirculation of the lungs; small aortic knob.

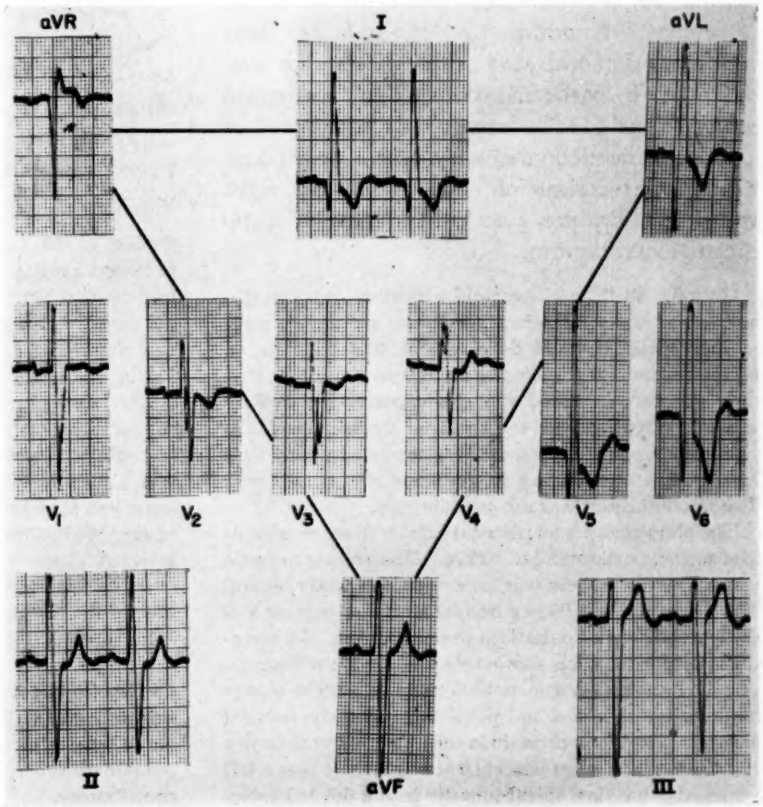



Fig. 5. Case 2. Electrocardiogram. Note the rather marked degree of left ventricular hypertrophy. The relatively tall R wave in $V_1$ also suggests concomitant right ventricular hypertrophy. Tracing was taken at full standardization to particularly emphasize the magnitude of the Q waves in $V_5$, $V_6$ and aVL; consequently, some of the R waves are foreshortened. These prominent Q waves suggest hypertrophy of the interventricular septum.

trophy (Fig. 5). Albuminuria was noted intermittently during episodes of congestive heart failure. *Roentgen examination* confirmed the marked cardiac enlargement. The left ventricle and left atrium were greatly enlarged and the aortic pulsations were hyperdynamic. The pulmonary artery segment was enlarged and the intrapulmonary vascularity increased (see Fig. 4).

*Cardiac catheterization* at the age of 13 years revealed the following:

| | *$O_2$ content vol. %* | *Pressure mm Hg* |
|---|---|---|
| Superior vena cava | 9.9 | 4 |
| Right atrium | 9.3 | 4 |
| Right ventricle | 12.8 | 45/2 |
| Main pulmonary artery | 12.0 | 45/23 |
| Left pulmonary artery | 11.7 | 45/24 |
| Right pulmonary artery | 12.3 | 45/23 |

The cardiac catheter failed to enter a patent ductus arteriosus despite repeated exploration of the pulmonary arteries. The arterial oxygen saturation was 94%.

A venous *angiocardiogram* at the age of nine years did not reveal any recognizable abnormalities. At the age of 15 years *retrograde aortography* was performed through a catheter inserted into the left brachial artery. This study did not reveal any contrast material in the lesser circulation.

*Comment:* This patient's physical signs were dominated by the presence of marked aortic insufficiency. In addition a definite left to right shunt was demonstrated at the ventricular level by cardiac catheterization. The aortogram served to exclude the presence of a patent ductus arteriosus, aorticopulmonary septal defect and rupture of the sinus of Valsalva into the right ventricle. Truncus arteriosus was excluded by the angiocardiogram.

Case 3. R. R., a 12-year-old white boy, was first discovered to have a cardiac murmur at the age of eight months. His physical development was poor as an infant but improved after the age of two years. At that time the parents noted that his capacity for exercise was decreased because of exertional dyspnea, and this symptom persisted. Cyanosis was not noted at any time and there was no history suggestive of rheumatic fever. The family history was not contributory.

The abnormalities on physical examination were localized to the cardiovascular system. The venous pressure was normal and there was no evidence of heart failure. The pulse rate was 90 per min, the rhythm regular and the femoral arterial pulsations were easily felt. All accessible peripheral pulses showed signs of a wide pulse pressure including Corrigan pulsations in the neck, water-hammer radial pulses and pistol shots over the femoral arteries. The blood pressure in the upper extremities was 120/50–0. The heart was enlarged and there was a left ventricular heaving apical impulse in the 6th left intercostal space in the anterior axillary line. A coarse systolic thrill was palpable maximally in the 4th and 5th left parasternal spaces. A harsh grade IV pansystolic murmur was audible maximally at the site of the thrill but radiated widely over the whole precordium. The 2nd heart sound was split. A grade III blowing diastolic murmur was audible maximally down the left sternal border. The rest of the examination was noncontributory.

*The electrocardiogram* showed evidence of left ventricular hypertrophy. *Roentgen examination* of the chest confirmed the cardiac enlargement which was predominantly of the left ventricle. The pulmonary artery segment was prominent and the intrapulmonary vascularity increased. The aorta was prominent, pulsated vigorously and was normal in position.

The results of *cardiac catheterization* were as follows:

| | *$O_2$ content vol. %* | *Pressure mm Hg* |
|---|---|---|
| Superior vena cava (1) | 15.9 | — |
| Superior vena cava (2) | 15.6 | — |
| Right atrium (high) | 15.5 | 7/3 |
| Right atrium (mid) | 14.7 | 7/3 |
| Right ventricle (mid) | 17.5 | 55/3–7 |
| Right ventricle (outflow) | 17.6 | 55/3–7 |
| Main pulmonary artery | 17.3 | 56/33 |
| Right pulmonary artery | 17.3 | 56/33 |
| Arterial oxygen saturation | 96% | |

*Comment:* This study demonstrated the presence of arterialized blood in the right ventricle consistent with ventricular septal defect. The blowing diastolic murmur along the left sternal border, in association with the signs of a wide pulse pressure, was suggestive of associated aortic valve incompetence.

Case 4. M. B., a 5-year-old white female, was found to have a cardiac murmur at the age of six weeks. During the first year of life she was asymptomatic and in particular did not have recognizable effort dyspnea or cyanosis and was free of recurrent pulmonary infections. During the second year of life effort dyspnea was noted. At that time physical examination revealed no evidence of congestive heart failure. The peripheral pulses were bounding. The blood pressure in the upper extremities was 120/40 and in the lower extremities 140/40. The heart was enlarged with a left ventricular apical impulse in the 5th left intercostal space in the anterior axillary line. A coarse systolic thrill was palpable maximally over the third left parasternal space but radiated widely toward the left clavicle and down the left sternal border. A harsh grade IV systolic murmur waxing in late systole was audible over the pulmonary area but radiated over the whole precordium. The 2nd heart sound was obscured by the systolic murmur and this was followed by a harsh grade II diastolic murmur maximal over the pulmonary area. The rest of the examination was noncontributory.

*Operative Findings:* Because of the typical machinery murmur, wide pulse pressure and cardiomegaly, the child was subjected to thoracotomy with the preoperative diagnosis of patent ductus arteriosus. The pulmonary artery was found to be two to three times its normal diameter and its pressure was palpably high. A patent ductus arteriosus with an inner diameter of 2 mm was divided and ligated. Following this there was little change in the systolic thrill along the main pulmonary artery. Further examination revealed that the maximal site of the thrill was on the anterior surface of the right ventricle about 2 cm below the pulmonary valve. Examination of the origin of the aorta and pulmonary artery was unsatisfactory but no abnormal structures were identified.

*Further Course:* About six months after surgery the child had repeated episodes of left heart failure which were usually precipitated by a mild respiratory infection. At that time it was noted that the cardiac murmurs had changed. The systolic murmur remained harsh and grade IV in intensity. It was followed by a split 2nd sound with accentuation of the pulmonary element. A blowing diastolic murmur followed the 2nd sound and was audible in the 2nd right and left parasternal spaces and down the left sternal border. At the apex a rumbling grade II mid-diastolic murmur was audible. Signs of a wide pulse pressure persisted.

*Roentgen examination* of the chest (Fig. 6) confirmed the presence of cardiomegaly with disproportionate enlargement of the left ventricle. The pulmonary artery segment was prominent and the intrapulmonary vascularity increased. The aorta was hyperdynamic. The *electrocardiogram* showed evidence of left ventricular hypertrophy.

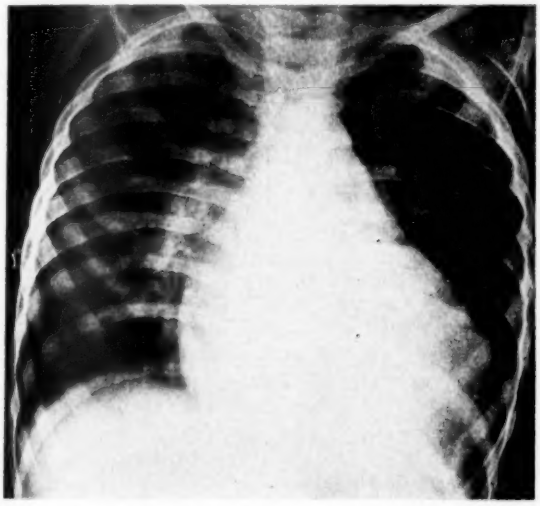


Fig. 6. Case 4. PA teleo of chest (8-18-54). There is marked increase in the transverse diameter of the heart predominantly toward the left. No significant prominence of the pulmonary artery segment or its branches. Aortic knob not significantly abnormal. Lung markings at the upper limits of normal.

*Comment:* Since thoracotomy, the major signs have been those of aortic insufficiency with an intracardiac left to right shunt. The present findings suggest that the shunt is at the ventricular level.

Case 5. J. B., a 20-year-old white female, was admitted to the hospital on March 9, 1955. A heart murmur was known to be present since the age of 14 months. The patient had no symptoms as a child, and specifically had no dyspnea, orthopnea, squatting, edema, cyanosis, hemoptysis, or cough. She did bicycling and roller skating, but refrained from taking classes in gymnastics in school. Growth and development were normal.

In October 1954, she developed left pleuritic pain. A roentgenogram of the chest at this time revealed an enlarged heart, and she was referred for cardiac diagnosis.

*Physical Findings:* On examination there was no cyanosis, clubbing of the fingers or abnormal venous pulsations. All peripheral arterial pulsations were vigorous. Examination of the lung fields revealed no abnormalities. The pulse was 100 per min. The blood pressure was 130/60 in the left arm and 170/60 in the right leg. The apical impulse was located in the 5th left intercostal space in the anterior axillary line. The rhythm was regular. There was a systolic thrill at the apex and at the pulmonic area. A grade III systolic murmur was present at the apex, along the left sternal border and at the pulmonic area and was transmitted to the lung bases posteriorly.

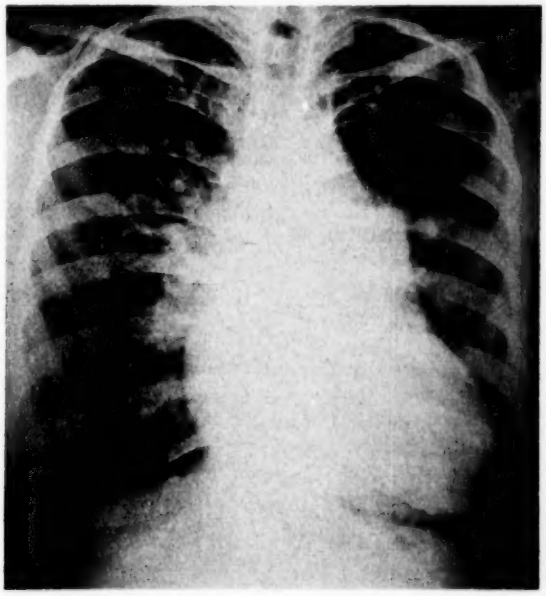


Fig. 7. Case 5. PA teleo of chest (2-16-55) showing prominent pulmonary artery segment and overcirculation of the lungs, normal or slightly enlarged aortic knob, and moderate increase in the transverse diameter of the heart to the left.

A grade II systolic murmur was present at the aortic area and transmitted along the carotid vessels. A grade II early diastolic murmur was heard at the pulmonic area. The aortic 2nd sound was diminished while the pulmonic 2nd sound was intensified. The remainder of the physical examination was not remarkable.

Laboratory studies: R.B.C.—4,540,000; hemoglobin —13.8 g; W.B.C.—5,100 with normal differential. Urinalysis was negative.

*Fluoroscopic and radiographic examination* of the chest (Fig. 7) revealed the transverse diameter of the heart to be increased moderately toward the left. The main pulmonary artery segment was rather strikingly enlarged as were its right and left main branches and the branches throughout the lungs. However, there was no evidence of abnormal pulsation of the pulmonary artery branches. There was overlap of the spine by the left ventricle up to 80 degrees of rotation into the left oblique. The aorta and its esophageal imprint were within normal limits. Cardiac and aortic pulsations appeared to be of the collapsing type. There was no evidence of left atrial enlargement but there was a suggestion of right ventricular enlargement as seen in the anterior clear space in the lateral view. No intracardiac calcification was noted. Apart from the overcirculation, the lungs appeared normal.

The *electrocardiogram* showed the pattern of left ventricular hypertrophy and, in addition, relatively tall R waves in lead $V_1$ suggested the presence of concomitant right ventricular hypertrophy.

*Cardiac catheterization* was performed on March 10, 1955. During the procedure complete right bundle branch block developed and continued throughout the duration of the catheterization. Four days later the tracing reverted to the pre-catheterization pattern. Results of the cardiac catheterization were as follows:

| | *$O_2$ content vol. %* | *Pressure mm Hg* |
|---|---|---|
| Superior vena cava | 11.79 | — |
| Right atrium (high) | 11.79 | 2 |
| Right atrium (low) | 10.95 | 2 |
| Right ventricle (inflow) | 12.11 | 50/8 |
| Right ventricle (outflow) | 12.34 | 54/2–5 |
| Pulmonary artery | 14.86 | 52/43 |
| Brachial artery | 16.39 | 122/53 |

| | |
|---|---|
| Arterial $O_2$ saturation | 97% |
| Pulmonary flow | 20.36 *l*/min |
| Systemic flow | 7.05 *l*/min |
| Left to right shunt | 12.31 *l*/min |

*Comment:* The physical findings in this patient were consistent with the diagnosis of ventricular septal defect and aortic insufficiency. Cardiac catheterization revealed some degree of pulmonary hypertension and an increase in oxygenation in the right ventricle over that in the right atrium and a second rise in the oxygen saturation in the pulmonary artery. This finding has been previously observed in this syndrome and while not diagnostic is again consistent. The significance of this so-called "double gradient" is discussed in the section entitled *Difficulties in Diagnosis*, page 548.

CASE 6. H. M., a 34-year-old white male, gave a history of heart disease since the age of six weeks, at which time a heart murmur was detected. His early development appeared normal. There was no history of cyanosis but fatigue and shortness of breath were noted in childhood, the dyspnea becoming more marked during his early teens. He was unable to finish college because of increasing exertional dyspnea. He had slept on three pillows most of his life, and had paroxysmal attacks of irregularity of the heart. These attacks might occur as often as every week and again be quite infrequent. The attacks would usually last from a few hours to four days, but would subside spontaneously. About three days prior to admission, while carrying some heavy objects, he began to notice that his heart was beating fast. He felt fatigued and had a "blackout spell." He was seen by a physician at home and referred to the hospital.

*Physical Findings:* The pulse was grossly irregular with an apical rate of 100 and he was having moderate chest discomfort due to palpitation. The respiratory rate was 30. There was no neck vein distention. Pulses were good in all extremities. The blood pressure ranged from 110/30 to 135/60. The apical impulse was in the 6th left interspace in the anterior axillary line. A systolic thrill was palpable in the 3rd interspace just to the left of the sternum and a grade IV high-pitched, blowing diastolic murmur was heard along the left sternal border maximally in the 4th interspace. The remainder of the physical examination was essentially negative.

An *electrocardiogram* showed left ventricular hypertrophy and frequent premature auricular contractions. The arrhythmia was controlled with quinidine.

*Roentgenographic studies of the chest* showed contraction of the ribs on the left, particularly over the upper half of the left thorax. The vascular markings of the left lung were fewer in number and smaller than on the right, and the heart was deviated to the left. There was a suggestion of slight elevation of the left diaphragm. The right lung showed evidence of over-circulation with a large pulmonary artery but no evidence of abnormal pulsation. The aortic knob and imprint were relatively large. There was evidence of disproportionate left ventricular enlargement with no evidence of left auricular or right sided enlargement. The antero-posterior diameter of the heart was not significantly increased but the heart was moderately enlarged in transverse diameter. A defect, extrinsic in nature, was seen on the anterior surface of the esophagus below the carina. Pulsations were forceful here and a shadow believed to be right pulmonary vein near its entrance into the left auricle was seen immediately adjacent to the defect. Pulsations of the aorta and left heart border were of the collapsing

type and there was an irregularity in rhythm. No intracardiac calcifications were seen. It was the impression of the roentgenologist that there was congenital absence of the left pulmonary artery, left ventricular enlargement and aortic insufficiency.

*A spirogram* revealed a vital capacity of 61 per cent of the predicted value and a maximal breathing capacity of 35 per cent of the predicted value. A *ballistocardiogram* showed complexes of the early M type during inspiration and of the late M type during expiration. The tracing was interpreted as being definitely abnormal. Urinalysis, blood count, and sedimentation rate were normal.

*Cardiac catheterization* was attempted. After the catheter was introduced into the right auricle, marked widening of the QRS complexes and disappearance of the P waves occurred. This was interpreted as nodal rhythm type 2 with left bundle branch block. The catheter was withdrawn before it entered the right ventricle but the arrhythmia continued. The left bundle branch block had disappeared by the following day but first degree A-V block was noted.

Arterial oxygen saturation was 96 per cent.

*Comment:* The clinical features of this patient were consistent with the diagnosis of a ventricular septal defect with aortic insufficiency. However, this diagnosis was only presumptive because cardiac catheterization was not successful and angiocardiography was refused.

CASE 7. J. D., a 6-year-old white boy, had had known congenital heart disease since the age of one year. He had respiratory distress with cyanosis for one hour after delivery and during the first year of life experienced choking spells after feedings. At the age of three years congestive heart failure developed. At the age of $3^1/_2$ years he was catheterized at the University Hospital in Birmingham, Alabama, by Dr. Richard Bing. The results of these studies performed May 11, 1955 are reported through the kind permission of Dr. Bing.

| | *Oxygen content vol. %* | *Pressure mm Hg* |
|---|---|---|
| Innominate vein | 7.50 | — |
| Superior vena cava | 7.83 | — |
| Right atrium | 7.83 | — |
| Right ventricle | 11.10 | 22/16/0 |
| | 10.87 | — |
| Main pulmonary artery | 10.55 | 31/24 |
| Right pulmonary artery | 10.30 | — |
| Pulmonary wedge | 14.10 (90.3% saturated) | 14 |

A diagnosis of ventricular septal defect with aortic insufficiency was made at that time.

In September 1955, at the University Hospital in Birmingham, he underwent a Cooley procedure for repair of the septal defect but it was thought that an adequate closure was not obtained. Postoperatively he ran a febrile course and had rapid heart action with decompensation. Numerous blood cultures were negative and it was thought that pulmonary atelectasis or consolidation was the most probable cause. He was discharged in November 1955.

He was first seen at the Cardiac Clinic at Grady Memorial Hospital, Atlanta, Georgia, in the fall of 1956. During the previous few months he had suffered from constant orthopnea and nonparoxysmal nocturnal dyspnea. He had occasional bouts of cyanosis although these episodes were less frequent since surgery. He had been on digitalis, low-salt diet and diuretics.

*Physical examination* revealed no cyanosis or clubbing. There was marked forward displacement of the sternum. The blood pressure was 180/0. The heart was enlarged with evidence of both right and left ventricular hypertrophy. There was a systolic thrill felt maximally in the 3rd left interspace. Loud systolic and diastolic murmurs, not continuous, were heard in the pulmonic area and an early blowing diastolic murmur was heard to the left of the sternum. The lungs were clear. The liver was palpable a hand's breadth below the right costal margin. There was no evidence of abdominal fluid.

*A chest x-ray* revealed marked cardiomegaly, increased vascularity of both lung fields and pulmonary congestion. On the lateral view there was rather marked thoracic cage deformity with precordial bulging.

*An electrocardiogram* was interpreted as showing first degree A-V block, right bundle branch block and possible right ventricular hypertrophy and auricular hypertrophy.

He was followed in the Cardiac Clinic in a state of chronic heart failure despite digitalis, low-salt diet and diuretics. Arterial oxygen saturation determination revealed a value of 86 per cent.

He was re-admitted to the Grady Memorial Hospital in December 1956, following a respiratory infection for control of heart failure and investigation for possible subacute bacterial endocarditis. Blood cultures, however, were negative.

He was subsequently followed in the Cardiac Clinic but was readmitted to the hospital in October 1957 because of another febrile episode accompanied by cough and respiratory distress and accentuation of his heart failure. He responded to therapy and has subsequently been followed in the clinic on the same regimen.

*Comment:* This patient's clinical findings, together with the demonstration of a left to right shunt at the right ventricular level by cardiac catheterization, are consistent with the diagnosis of ventricular septal defect and aortic insufficiency.

## REVIEW OF PREVIOUSLY REPORTED CASES

Ventricular septal defect with aortic insufficiency has been rather infrequently described in the literature.[1–28] Some cases have been

TABLE I

Autopsy-Proved Cases of Ventricular Septal Defect with Aortic Insufficiency

| Author Year | Age Sex | History | Thrills (site of maximal intensity) | Murmurs (site of maximal intensity) | B.P. | Electrocardiogram (continued on facing page) |
|---|---|---|---|---|---|---|
| Breccia[1] 1906 (a) | 46 M | No cardiac symptoms. Died of peritonitis | No | No | — | — |
| Laubry and Pezzi[2] 1921 | — | Sickly since childhood; crushing chest pain and heart failure present for many months before admission | Marked systolic 3 LIS | Systolic 3 LIS. Soft blowing diastolic LSB | 160 (systolic) (bounding pulse) | — |
| Laubry *et al.*[3] 1933 | 18 M | Heart disease diagnosed before age of 10 years; extreme dyspnea; congestive failure; cyanosis present when in failure | Faint diastolic LSB | Loud continuous with systolic accentuation upper sternum; diastolic component LSB | 135/45 | — |
| Brandeburg[4] 1934 cited by Brown[11] | — | — | — | — | — | — |
| Allen[7] 1941 | 15 F | Heart disease diagnosed at age of 7 years. Fever, chills, weakness for 3 weeks before admission. Blood culture positive strep. viridans | Coarse systolic and diastolic 2 LIS | Loud roaring to-and-fro, almost continuous with systolic accentuation 2 LIS | 130/20 | Sinus tachycardia; "myocardial disease" |
| Ascenzi *et al.*[15] 1951 | 21 F | Physical and mental development slightly retarded; since infancy assumed squatting position after exercise; transient cyanosis when 5 days old; cyanosis also occurred during winter | 4,5 LIS | Continuous 4,5 LIS | 125/20 | Left axis deviation |
| Edwards *et al.*[19] 1954 | 17 | — | — | "Machinery" like | — | — |
| Wood *et al.*[20] 1954 | 21 F | Heart disease known since age 1 year. Palpitation, fatigue, exertional dyspnea had always been present | Systolic 3,4 LIS | Loud pansystolic 3,4 LIS; long blowing diastolic | 110/50 | LVH |
| Philipson and Saltzman[21] 1955 | 26 M (case 4) | Congenital heart defect established in early infancy. Symptom-free until 5 months before admission when he developed fever | Strong thrill 4 LIS | "Systo-diastolic" 4 LIS | 160/50 | LV "strain" |
| Winchell and Bashour[24] 1956 | 57 M (case 4) | Dyspnea and edema, age 30 | — | Loud systolic and diastolic with to-and-fro character LSB | 160/0 | RBBB |
| | 33 M (case 6) | Heart murmur discovered at age 13 years. Congestive failure developed at age 30, followed by fever, purpura | To-and-fro LSB | Loud to-and-fro LSB | 160/60 | LVH; AF |
| Danaraj[26] 1956 | 14 F | (Chinese) Sudden onset of severe substernal pain. No prior history or diagnosis of heart disease | Continuous 2 LIS | Rough "machinery" type 2 LIS | — | — |
| Claypool *et al.*[27] 1957 | 5 F | Diagnosis of heart disease made at age of 1 month | Marked systolic 2 LIS | Grade 5 "machinery" type 2 LIS. Grade 2 apical diastolic rumble | 130/40–0 | LVH; possible RVH |

See page 541 for explanatory notes and key to abbreviations.

TABLE I (Continued)

Autopsy-Proved Cases of Ventricular Septal Defect with Aortic Insufficiency

| Chest x-ray or fluoroscopy | Arterial oxygen saturation | Cardiac catheterization: Oxygen content (vol. %) or saturation (%) RA | RV | PA | Cardiac catheterization: Pressure mm Hg RV | PA | Autopsy findings: Ventricular septal defect | Aortic valve cusps* |
|---|---|---|---|---|---|---|---|---|
| — | — | — | — | — | — | — | Triangular; high VSD | 2 mm linear fissure in right valve cusp |
| — | — | — | — | — | — | — | Oval, 1 cm diameter, located below right aortic cusp; edges thick, sclerotic | Valve cusps thickened; two fenestrated; posterior and right aortic cusps united by fibrous band |
| Marked cardiac enlargement | — | — | — | — | — | — | High, 1 cm diameter, beneath posterior cusp | Posterior cusp pulled down, retracted and everted by short, thick, fibrous band; cusp covered part of defect |
| — | — | — | — | — | — | — | High | Fibrosis in region of defect involved an aortic cusp and led to its deformity |
| Marked widening of contour of heart | — | — | — | — | — | — | Oval defect 1.5 x 1.2 cm in membranous septum. Bacterial vegetations on margin | Right cusp thickened, folded and protruding through VSD. Bacterial vegetations on right and posterior cusps (b) |
| Marked cardiac enlargement; hyperactive hilar vessels | — | Oxygen samples not reliable because of air bubbles | | | 45/5 | 33/20 | Round defect 1 cm diameter in membranous septum | Aortic valves thick, shrunken, deformed, especially posterior cusps. Cusp adjacent to IV septum had aneurysmal outpouching which bulged into VSD |
| Marked cardiac enlargement | — | — | — | — | — | — | Defect involving membranous septum | Deformity of right and posterior cusps |
| Markedly enlarged hyperdynamic left ventricle; slight pulmonary congestion | — | — | — | — | — | — | Oval defect in membranous septum 2 cm in length | Anterior cusp margins thickened and rolled; partly prolapsed into VSD |
| Enormous cardiac enlargement; dilatation of LV; moderate widening of pulmonary artery and branches; aorta normal caliber | — | 11.8 vol. % | 15.9 vol. % | 16.4 vol. % | 87 cm $H_2O$ | 94 cm $H_2O$ | Defect in membranous septum 24 mm diameter immediately below right aortic valve | All valves stretched and margins thickened, especially the right where in addition to marked thickening and lipping was a verrucose calcified deposit |
| Marked cardiac enlargement; prominent pulmonary vascular markings | 94% sat. | 65% sat. | 90% sat. | 89% sat. | 63/13 | 58/25 | Defect in membranous septum 1.5 × 0.5 cm immediately beneath right aortic cusp | Right aortic cusp displaced inferiorly, thickened; did not close completely (c)† |
| Marked cardiac enlargement; prominent pulmonary vascular markings | 95% sat. | 61% sat. | 82% sat. | 83% sat. | 70/0 | 80/30 | Defect in membranous septum 2.5 cm diameter, immediately below right aortic cusp | Right aortic cusp markedly displaced inferiorly, thickened and did not close adequately. Bacterial vegetations on aortic cusps |
| — | — | — | — | — | — | — | Circular defect 1 cm diameter directly below attachment anterior aortic cusp | Pouch-like dilatation of base of anterior aortic cusp; prolapsed into VSD (d)† |
| Marked cardiac enlargement. Markedly increased pulmonary vascular markings | 91% sat. | 10.78 vol. % | 13.28 vol. % | 12.81 vol. % | 80/0-7 | 82/43 | Defect 1 cm diameter in membranous septum | Noncoronary cusp hypertrophied and displaced inferiorly |

(*continued on next page*)

See page 541 for explanatory notes and key to abbreviations.

TABLE I (Continued)
Autopsy-Proved Cases of Ventricular Septal Defect with Aortic Insufficiency

| Author Year | Age Sex | History | Thrills (site of maximal intensity) | Murmurs (site of maximal intensity) | B.P. | Electrocardiogram |
|---|---|---|---|---|---|---|
| Paul *et al.*[29] 1957 | 21 M | (Further Details Not Available) | | | — | — |
| Scott *et al.* | 17 F | Heart murmur first noted at age 1 year. Kyphoscoliosis since childhood. Developed congestive failure age 13 | Systolic LSB | Harsh systolic 2 LIS. Loud blowing diastolic 2 LIS | 134/44 | Combined ventricular hypertrophy; AF |

See page 541 for explanatory notes and key to abbreviations.

proved by autopsy while in other instances the diagnosis has rested on physical, laboratory or surgical findings.

A résumé of the pertinent features of the cases with autopsy proof (including our first case) is given in Table I. Case 4 of Winchell and Bashour,[24] the case reported by Danaraj,[25] as well as the case of Espino-Vela and Mata[23] may possibly more correctly represent examples of congenital aneurysms of the sinuses of Valsalva with perforation into the right heart in association with ventricular septal defects.

In addition to these autopsy-proved cases are those in which the clinical diagnosis has been confirmed by cardiac catheterization,[10,20,24] angiocardiography,[10,21] or exploratory thoracotomy.[10,21,24] These include the first case of Soulié, Routier and Bernal,[10] the second case of Wood, Magidson and Wilson,[20] the first three cases of Philipson and Saltzman,[21] and cases 1, 2, 3 and 5 of Winchell and Bashour.[24]

Dexter and associates[8] described the catheterization findings in a case of ventricular septal defect. This six-year-old boy also had a diastolic murmur along the left sternal border, and a systemic blood pressure of 105/45. They stated that catheterization did not explain the low diastolic pressure or diastolic murmur and suggested that he probably had aortic insufficiency, but did not speculate as to the cause of the aortic insufficiency. This case may possibly represent an example of the syndrome under discussion.

Gross[18a,b] has called attention to this condition, stating that several patients were operated with the mistaken diagnosis of patent ductus arteriosus. He stated that he had seen 12 cases of high interventricular septal defect which lay in such a position that the medial cusp of the aortic valve was incompletely supported, and hence collapsed from time to time to give aortic regurgitation. He described the murmur as not intense in the pulmonary area and of a to-and-fro rather than a continuous quality. He observed a marked tendency for the murmur to change in character from time to time. His cases had very low diastolic pressures, important A-V conduction defects and greatly increased pulsations of the aortic arch and pulmonary artery. No autopsy findings were given.

Nadas[26] encountered two patients with aortic insufficiency among 62 children with ventricular septal defects. He stated, in addition, that five more had been operated with the presumptive diagnosis of patent ductus. He summarized the clinical, electrocardiographic, roentgenologic, and cardiac catheterization findings in this syndrome. In his experience these children were stunted and frail with left chest deformity. One patient had bacterial endocarditis.

TABLE I (Continued)

Autopsy-Proved Cases of Ventricular Septal Defect with Aortic Insufficiency

| Chest x-ray or fluoroscopy | Arterial oxygen saturation | Cardiac catheterization: Oxygen content (vol. %) or saturation (%) | | | Cardiac catheterization: Pressure mm Hg. | | Autopsy findings: Ventricular septal defect | Autopsy findings: Aortic valve cusps* |
|---|---|---|---|---|---|---|---|---|
| | | RA | RV | PA | RV | PA | | |
| — | — | — | — | — | — | — | High septal defect | — |
| Marked cardiac enlargement. Prominent pulmonary artery and pulmonary over-circulation | 96% sat. | 8.9 vol. % | 9.5 vol. % | 14.3 vol. % | 90/4 | 90/55 | Defect in membranous septum just below noncoronary cusp; crescent-shaped, 1.4 cm across when viewed from left ventricle, circular and 2 cm diameter when viewed from right ventricle | Noncoronary cusp unsupported; displaced slightly below superior margin of right and left aortic cusps |

AF—auricular fibrillation
LIS—left interspace adjacent to sternum
LSB—left sternal border
LV—left ventricle
LVH—left ventricular hypertrophy
PA—pulmonary artery
RA—right atrium
RBBB—right bundle branch block
RIS—right interspace adjacent to sternum
RSB—right sternal border
RV—right ventricle
RVH—right ventricular hypertrophy
VSD—ventricular septal defect

(a) Breccia's case[1] cannot be accepted unequivocally as an example of ventricular septal defect with aortic insufficiency because of the lack of clinical findings as well as the somewhat questionable demonstration at autopsy of aortic valve incompetence.

(b) Pathologic evidence of acute rheumatic valvulitis and myocarditis.

(c) Aneurysm of right sinus of Valsalva with three small fenestrations opening into right ventricle.

(d) Rupture of prolapsed pouch at apex; probe could be passed through it from left to right ventricle.

* The nomenclature of the three aortic valve cusps and their corresponding sinuses has been quite varied.[51] The currently preferred terms are right coronary, left coronary, and noncoronary cusps (and sinuses) as advocated by Jones and Langley.[51] However, in our review of the literature, the terms actually applied by the respective authors have been retained.

† These cases may possibly represent examples of congenital aneurysm of the sinus of Valsalva with perforation into the right heart in association with ventricular septal defect.

In addition, reference to this entity has been made by other authors without presenting any specific cases of their own.[5,12,14,17,29b] Becu and co-workers[30] in an autopsy study of 50 cases of ventricular septal defect encountered one case in which aortic insufficiency was also present. Further details, however, were not presented.

*Ventricular Septal Defect, Aortic Insufficiency, and Dextroposition of the Aorta:* Scattered cases of a similar syndrome have been reported.[6,9,10,13,16,22,23] These have been described as high ventricular septal defects with aortic insufficiency and slight dextroposition of the aorta and have been called Eisenmenger's complex. These cases probably should be included as examples of the present syndrome. Lesser degrees of dextroposition of the aorta are frequently difficult to diagnose even at the autopsy table.[29a,b] As has been pointed out by Becu and associates,[30] in ventricular septal defects which involve the septal tissue lying below the anterior half of the right aortic cusp, the aortic leaflets overhang the outflow tract of the right ventricle, giving the impression of "dextroposition" of the aorta. Consequently the presence or absence of a statement in case reports regarding slight dextroposition of the aorta cannot be used as a good means of subdividing this syndrome of high ventricular septal defect with aortic insufficiency. Therefore, we have chosen to include all such cases in this report.

The occurrence in ventricular septal defect of a right to left shunt (producing central cyanosis) has been proposed as a clinical means of diagnosing Eisenmenger's complex.[29a,b] It thus becomes more of a physiologic than a strictly anatomic diagnosis.[31] None of the cases with ventricular septal defect and aortic insufficiency that have been reported with men-

TABLE II

Autopsy-Proved Cases of Ventricular Septal Defect with Aortic Insufficiency and Dextroposition of the Aorta

| Author and year | Age and sex | History | Thrills (site of maximal intensity) | Murmurs (site of maximal intensity) | B.P. | Electrocardiogram (*continued on facing page*) |
|---|---|---|---|---|---|---|
| Taussig and Scmans[6] 1940 | 7 M | (Negro). Heart murmur detected 3 weeks before admission. Blood culture positive for Staph. aureus | Marked systolic RSB at base. Diastolic RSB | Very harsh systolic maximum over base close to sternum. Very loud ringing diastolic over sternum maximum on right | 112/0 | Three standard leads; no axis deviation |
| Hurst and Schemm[9] 1948 | 21 F | Congenital heart disease diagnosed at age 16 month. Recurrent respiratory infections; epistaxis; dyspnea; transient cyanosis when coughing; congestive failure | Systolic-diastolic 2 LIS | Loud machinery-like 2 LIS. Short systolic and diastolic 2 RIS | 145/80–50 | No axis deviation (at age 16) |
| Soulie *et al.*[10] 1949 | 13 F | Known acyanotic congenital heart disease since birth. Violent palpitation, exertional dyspnea of several months' duration | Systolic 3 LIS | Loud rough systolic 2,3 LIS. Loud diastolic 2 LIS | 125/0 | Combined hypertrophy but predominantly LVH |
| Ash and Murphy[13] 1950 | 3½ F | Heart murmur first heard at 3 months; congestive failure | Systolic 2–5 LIS | Rumbling, continuous 2 LIS. Systolic 2–5 LIS | 110/40–0 | — |
| Welti *et al.*[36] 1952 | 21 M | Heart murmur discovered at age 4 years. Severe arrested development, right arm. Pronounced kyphoscoliosis. Dyspnea, fever 5 months before admission; evidence of subacute bacterial endocarditis; blood culture positive Strep. viridans. Congestive failure | Systolic 2 RIS | Loud systolic 2 RIS. Diastolic 2 RIS and 3 LIS | 4–12 mm. Hg. diastolic | — |
| Bayliss *et al.*[33] 1955 | 9 M | Heart murmur first heard at age 8 months. Congestive failure | Systolic and diastolic upper chest | Rough to-and-fro below left clavicle | 140/50 | LVH |
| Espino-Vela and Mata[38] 1956 | 20 M (case 1) | Had always been well. One month before death had sharp precordial pain, cough, hemoptysis; congestive failure last month of life | Systolic and diastolic 2 LIS | Systolic and diastolic 2 LIS | 130/0 | LVH |

For key to abbreviations see Table I.

* See Table I for nomenclature of the three aortic cusps and their corresponding sinuses.

† This case may possibly represent an example of congenital aneurysm of the sinus of Valsalva with perforation into the right heart in association with ventricular septal defect.

tion of dextroposition of the aorta have had cyanosis (except one case in which transient cyanosis was noted during paroxysms of coughing[9]). In fact, it thus becomes debatable whether

TABLE II (Continued)

Autopsy-Proved Cases of Ventricular Septal Defect with Aortic Insufficiency and Dextroposition of the Aorta

| Chest x-ray or fluoroscopy | Arterial oxygen saturation | Cardiac catheterization: Oxygen content (vol. %) or saturation (%) | | | Cardiac catheterization: Pressure mm Hg | | Dextroposition of aorta | Autopsy findings: Ventricular septal defect | Autopsy findings: Aortic valve cusps* |
|---|---|---|---|---|---|---|---|---|---|
| | | RA | RV | PA | RV | PA | | | |
| Markedly enlarged "boot shaped" heart | — | — | — | — | — | — | Slight | Defect 1.75 cm in diameter immediately beneath right aortic cusp. Minute vegetations along lower margin; acute endocarditis of VSD | Right aortic cusp thickened; line of closure retracted, lay at lower level; adherent at both insertions to adjacent cusps. Right and left sinuses of Valsalva greatly increased in size |
| Heart greatly enlarged; pulmonary arc segment enlarged; small aortic knob | — | — | — | — | — | — | Slight | Crescent-shaped defect 2 x 0.6 cm at base of right aortic cusp | Right aortic cusp sacculated; free margin thickened and calcified; in diastole cusp carried down into ventricle to partly occlude VSD |
| Enormous heart, especially L.V. Pulmonary arc segment pulsated vigorously; enlarged right hilum | 95% sat. | 9.29 vol. % | 10.48 vol. % | 13.10 vol. % | — | 40 (diastolic) | Moderate | Defect 25 mm diameter limited below by a semilunar band | Posterior and right anterior cusps thickened and moderately dextroposed. Semilunar band inserting into middle of posterior cusp retracted it downward |
| Marked cardiac enlargement; fullness in pulmonary area | — | — | — | — | — | — | Slight | High defect, 0.8 x 1.1 cm | Aneurysmal dilatation of posterior cusp and sacculation of right anterior cusp with protrusion downward and septalward of both cusps through VSD |
| — | — | — | — | — | — | — | Definite | High defect in membranous septum immediately above right anterior cusp | Right anterior cusp hypertrophied; thickened, free edge thought to evert during diastole. Vegetations on right and left anterior cusps |
| Enormous cardiac enlargement; aorta large and pulsatile; no hilar dance | 98% sat. | 60% sat. | 67% sat. | 87% sat. | 75/0 | 55/25 | Aorta appeared to arise chiefly from right ventricle | High defect 20 x 12 mm | Anterior aortic cusp greatly ballooned; large anterior cusp displaced downward and covered VSD |
| Cardiac enlargement with slight prominence of pulmonary arc segment and increased vascular markings | — | — | — | — | — | — | Slight | High defect 23 mm in greatest diameter | The aortic cusp overriding the septum was enlarged and fenestrated† |

these cases are technically Eisenmenger's syndrome or not. Be that as it may, we have included them as examples of the present syndrome of ventricular septal defect with aortic insufficiency. This is in accord with the concept of Selzer and Laqueur[29b] that these cases more properly should be regarded as simple ventricular septal defect with aortic regurgitation.

A summary of these cases is presented in Table II.

## Differential Diagnosis

### CASES WITH SHUNTS

*Ventricular Septal Defect without Aortic Insufficiency:* A diastolic murmur along the left sternal border has been described in ventricular septal defects without aortic insufficiency.[17,20,29a,b,32–34] This murmur is usually soft and blowing and is thought to be the result of pulmonary valve insufficiency secondary to pulmonary hypertension.[14,20,29a,b,31] In these cases the systemic diastolic pressure is not low, as it is in the syndrome under discussion. A lesser degree of associated aortic valve incompetence cannot be ruled out in some of these reported cases[14,32–34] as autopsy confirmation was not presented.

*Ventricular Septal Defect with Acquired Aortic Insufficiency:* A ventricular septal defect with acquired aortic insufficiency may be difficult or impossible to differentiate from the present syndrome. In fact, Selzer[29a] described two such cases which ran a febrile course, had wide pulse pressures, and which at autopsy showed bacterial endocarditis of the aortic valves. (See also the section on *Bacterial Endocarditis*, page 547.)

*Ventricular Septal Defect and Bicuspid Aortic Valve:* Ventricular septal defect with bicuspid aortic valve and complicating aortic insufficiency will produce a clinical picture indistinguishable from that of the present syndrome, nor will cardiac catheterization or angiography help to make this distinction.

*Patent Ductus Arteriosus:* Patent ductus arteriosus occasionally may be confused with the present syndrome. In both, the systemic arterial pressure is wide. In ventricular septal defect with aortic incompetence the diastolic murmur tends to be maximal along the left sternal border, although in some instances the murmur may be continuous.[3,9,10,13,15,19,25,26] Conversely, the murmur of patent ductus may occasionally have a to-and-fro character rather than a continuous one. In such cases distinction by auscultation alone is virtually impossible. In patent ductus with large left to right shunts, the electrocardiogram usually shows left ventricular hypertrophy.[14,18a,31] Cardiac catheterization may permit the correct diagnosis to be made since there is a rise in oxygen content in the blood obtained from the pulmonary artery over that obtained from the right ventricle, although even this finding is not absolutely conclusive. (See the section *Difficulties in Diagnosis*, p. 548.) Passage of the catheter through the patent ductus and into the descending aorta will establish the correct diagnosis. Similarly, an aortogram will usually permit the demonstration of the ductus.

In the *syndrome of patent ductus with severe pulmonary hypertension*[35–37] the typical Gibson murmur is often absent and a systolic and diastolic murmur may be present (or no murmurs at all or only a systolic or a diastolic murmur). The diastolic murmur in these cases is thought probably to represent pulmonary valve incompetence.[36] On physical examination the features of pulmonary hypertension dominate the picture. Cyanosis is often present and may be confined to the lower extremities. The pulse pressure may be normal or wide.[37] The electrocardiogram usually shows right ventricular or bi-ventricular hypertrophy. At cardiac catheterization, there often will be an increase in oxygen content of blood obtained from the right ventricle over that obtained from the right auricle. In these cases this is probably due to the pulmonic valve insufficiency with regurgitation of blood from the pulmonary artery into the right ventricle. Usually, however, the catheter can be passed through the ductus, thus permitting the correct diagnosis to be made. Angiocardiography will show early filling of the descending aorta from the pulmonary artery in those cases where the pulmonary artery pressure is sufficiently high to cause reversal of flow. Simultaneous sampling of right brachial and femoral arterial blood is perhaps the best means of diagnosing this condition and of distinguishing it from the present syndrome. In patent ductus with pulmonary hypertension and reversal of shunt, there will be unsaturation of the femoral arterial sample. Dye dilution curves will also demonstrate a right to left shunt at the level of the pulmonary artery.

Another condition that must be considered in differential diagnosis is that of *patent ductus with an abnormal aortic valve*.[38] In this condition, in addition to the continuous ductus murmur, a

blowing diastolic murmur (differing in pitch from the diastolic component of the continuous murmur) may be heard along the left or right sternal border. A systolic thrill and murmur to the right of the sternum are often also present.[38] The electrocardiogram usually shows left ventricular hypertrophy.

*Patent Ductus and Ventricular Septal Defect:*[17,30,39] Another combination of defects which may be difficult to distinguish from the present syndrome is that of ventricular septal defect associated with a patent ductus arteriosus. Of 50 autopsied cases of ventricular septal defects reported by Becu and associates,[30] five had an associated patent ductus arteriosus.

Bowers, Burchell and Wood[39] described the catheterization findings in a 14-year-old girl with this combination of abnormalities. In this case there was an increase in the oxygen content of the right ventricular blood over that in the right atrium and of the pulmonary artery blood over that in the right ventricle. Definite confirmation of the diagnosis can be obtained if the catheter traverses the patent ductus.

*Aortopulmonary Septal Defect:*[40–46] An aortopulmonary septal defect is frequently clinically indistinguishable from patent ductus,[12,43] and occasionally from ventricular septal defect.[43,45] Consequently, it may at times be confused with ventricular septal defect and aortic insufficiency. The murmur is often described as continuous but Azevedo and associates[46] found that in 40 per cent of patients the murmur was "systo-diastolic" and in 35 per cent the murmur was systolic only. The murmur of aortopulmonary septal defect has been described as more superficial than that of patent ductus[40] and more medial and lower[42,44] but this is frequently not of differential value.[12,44] The pulse pressure is usually wide.[42] The roentgen picture is ordinarily not diagnostic.[41,44,46] The electrocardiogram likewise may not be of differential value.[41,42,45,46]

Cardiac catheterization will show evidence of a left to right shunt into the pulmonary artery but this does not distinguish it from patent ductus. Passage of the catheter through the aortopulmonary defect and assurance that it courses anteriorly and has not entered the aorta through a ventricular septal defect is evidence of an aortic septal defect.[43] D'Heer and Van Nieuwenhuizen[45] described a method for correctly diagnosing aortopulmonary septal defect by cardiac catheterization. By manipulation of the catheter first toward the aortic arch and then toward the aortic valve, and superimposition of the x-ray films showing two catheter positions, a defect in the ascending aorta could be demonstrated. Further confusion with ventricular septal defect occurs when pulmonary hypertension[43,46] and associated pulmonic valve insufficiency result in increased oxygenation in the right ventricle.[43]

Retrograde aortography[43,44,46] is the method of choice for the diagnosis of aortopulmonary septal defect and will accurately demonstrate the site of the shunt.

*Aortopulmonary Septal Defect and Ventricular Septal Defect:* The combination of aortopulmonary septal defect and ventricular septal defect may be very difficult to distinguish from the present syndrome. (See section *Difficulties in Diagnosis*, page 548.)

*Ruptured Aneurysm of the Sinus of Valsalva:*[47–62] Rupture of an aneurysm of the sinus of Valsalva into the right side of the heart must also be considered in differential diagnosis. This clinical syndrome has been well-defined by Oram and East.[47] It more commonly occurs in males who have frequently had no prior evidence of heart disease. Usually there is sudden severe chest pain and the appearance of a continuous or to-and-fro murmur (often with a thrill) heard maximally near the center of the sternum and in the left 2nd to 4th interspaces. In Wood's case[12] the continuous murmur and thrill were maximal in the 4th intercostal space. This was also true in the case described by Brown, Heath and Whitaker.[50] When the rupture occurs into the right atrium the to-and-fro murmur is usually maximal over the lower sternal region and the diastolic component is often transmitted down the right sternal border.[48] The pain usually subsides after a few days and dyspnea and right heart failure appear. A wide pulse pressure and systolic pulsations of the cervical veins and liver are frequent.

The diastolic component of the murmur is thought to be due to the flow of blood through the perforated aneurysm or to an actual aortic

valve insufficiency due to distortion of one or more of the aortic valve cusps by the aneurysm (see below). The electrocardiogram is usually not of differential value,[47] although some authors[49,62] have stated that the presence of right axis deviation associated with aortic insufficiency is of diagnostic help. In other cases[19,50] left ventricular hypertrophy was present.

A subgroup includes those patients with ruptured sinus of Valsalva aneurysms and a deformed aortic valve cusp. The aortic insufficiency in these cases may be due to distortion of the aortic leaflet by the aneurysm or to an anomaly of the aortic cusp such as a bicuspid valve.[51]

Another subgroup of the cases of ruptured aneurysm of the sinus of Valsalva includes those with an associated ventricular septal defect.[30,51–54,62] Morgan and Burchell[55] reported a case with cardiac catheterization data which they thought represented an instance of ventricular septal defect and aortic insufficiency.* However, at autopsy,[56] this case proved to be an aneurysm of the sinus of Valsalva which communicated through a perforation into the right ventricle. In addition there was an associated ventricular septal defect. Case 4 of Winchell and Bashour[24] may be an example of this entity as may possibly also be the cases of Danaraj[25] and of Espino-Vela and Mata[23] (Tables I and II).

There may be great difficulty in differentiating a ventricular septal defect with aortic insufficiency from a communication between an aortic sinus aneurysm and the right heart which has been present from birth because in the latter case the advantage of the characteristic history of rupture is lacking.[51] This is well exemplified by the case of Burchell and associates.[55,56]

In ruptured aneurysm of the sinus of Valsalva cardiac catheterization will show an increase in oxygen in that chamber of the heart into which the perforation has occurred.[19,50,52,57] In Burchell's case which had an associated ventricular septal defect the precise anatomic diagnosis could not be made from the catheterization data because both the septal defect and the perforated sinus of Valsalva aneurysm were causing a left to right shunt at the level of the right ventricle.[55,56]

Retrograde aortography is of help in the differential diagnosis in demonstrating the localization of the rupture, although it is not without danger.[52] Even with this technic an absolute distinction between ruptured aneurysm of the sinus of Valsalva into the right ventricle with (or without) an associated ventricular septal defect and the syndrome of ventricular septal defect with aortic insufficiency cannot always be made.

*Rupture of Aortic Aneurysm Into the Pulmonary Artery:* This syndrome has been well described and is usually due to syphilis.[63–70] There is often a history of the sudden onset of chest pain followed by increasing dyspnea, right heart failure and the presence of a continuous or (occasionally) a to-and-fro murmur in the 2nd or 3rd interspace to the left of the sternum, often accompanied by a thrill. The pulse pressure is wide. The electrocardiogram usually shows right axis deviation or right ventricular hypertrophy.[64,68,70] Fluoroscopically there is marked fullness in the region of the pulmonary arc segment and increased pulsation of the hilar vessels.

Differentiation from ventricular septal defect with aortic insufficiency should not be especially difficult. The history of sudden onset of symptoms, the positive serology and the roentgen evidence of an aneurysm of the aorta may suffice to make the distinction. Cardiac catheterization[66,68] will reveal an increase in oxygenation in the pulmonary artery and increased pressure in the right ventricle and pulmonary artery. However, if pulmonic valve insufficiency exists there may also be an increase in oxygen saturation in the right ventricle, which will confuse the picture. Aortography, the patient's condition permitting, will demonstrate the site of the aorticopulmonary fistula.

*Rupture of Aortic Aneurysm Into the Superior Vena Cava:*[71] This rare condition affects males predominantly in the fifth and sixth decades and is usually due to syphilis. Rupture is usually accompanied by the rather sudden onset of chest pain and/or dyspnea and the signs of superior vena caval obstruction appear. A loud continuous or to-and-fro murmur is heard, usually to the right of the sternum in the second interspace but occasionally to the left of the sternum.

* This case has been erroneously perpetuated in several articles as an example of ventricular septal defect with aortic insufficiency.

A wide pulse pressure may be present. Chest x-ray demonstrates an aneurysmal mass protruding to the right from the ascending aorta or arch. Usually the clinical picture is sufficient to make the diagnosis although cardiac catheterization or aortography may be required.

*Coronary Arteriovenous Fistula:*[72–76] This relatively rare anomaly will produce a continuous murmur. The coronary arterial blood may be shunted directly into the coronary sinus, right ventricle, or pulmonary artery.[76] The pulse pressure is usually not wide although it was increased in the case of Davison and associates.[75] Cardiac catheterization will show a marked increase in oxygen saturation in the right heart at the level of the fistulous communication.

*Truncus Arteriosus:*[31,77,78] Truncus arteriosus, which is always associated with a ventricular septal defect, may give rise to a continuous machinery type murmur or a murmur resembling aortic insufficiency. This may present a difficult differential diagnosis especially since some cases may show left ventricular hypertrophy.[77]

The pulse pressure may be wide. Roentgenograms show a deep concavity at the site of the pulmonary arc. Final distinction is usually possible by means of cardiac catheterization and/or angiocardiography.

CASES WITHOUT SHUNTS*

*Rheumatic Aortic Insufficiency:* Rheumatic aortic insufficiency alone or in combination with aortic stenosis may at times be difficult to distinguish from the present syndrome. There is a loud blowing diastolic murmur over the aortic area and along the left sternal border together with peripheral signs of aortic insufficiency. In aortic insufficiency associated with aortic stenosis and also in severe pure aortic insufficiency[79] there is a loud systolic murmur over the aortic area. Cardiac catheterization will establish the absence of a left to right shunt.

*Syphilitic Aortic Insufficiency:* In syphilitic aortic insufficiency are encountered loud blowing diastolic murmurs over the aortic area and along the left sternal border and frequently also a loud systolic murmur over the aortic area[79] together with peripheral signs of aortic insufficiency.

A history of syphilis, a positive serology, or radiographic evidence of aneurysm or calcification in the ascending aorta in an individual under the age of 50 usually serves to establish this diagnosis.[80]

*Bacterial Endocarditis:* Bacterial endocarditis may attack the aortic valve and cause destruction of a portion of the cusps with resultant aortic regurgitation. While occasionally bacterial endocarditis attacks a previously normal valve, more commonly the aortic valve is already abnormal as from rheumatic involvement or a congenital bicuspid valve. Such cases at times may be confused with the present syndrome but careful history and physical examination, together with the rather rapid appearance of severe aortic insufficiency, a febrile course, and the presence of positive blood cultures point to the correct diagnosis. It should be emphasized, however, that bacterial endocarditis may on occasion be engrafted on the septal defect or the deformed aortic valve cusp in the present syndrome[7,16,21,24,26] and thus may make the differential diagnosis more difficult.

*Unruptured Aneurysm of the Sinus of Valsalva:* Occasionally an unruptured aneurysm of the sinus of Valsalva may produce to-and-fro or continuous murmurs. The aneurysm may protrude into the outflow tract of the right ventricle or compress the pulmonary artery giving rise to systolic bruits. Dilatation of the aortic valve ring, distortion of the aortic cusps by the aneurysm or associated anomalies of the aortic cusps may produce peripheral signs of aortic insufficiency.[51,81,82] Cases such as this have been reported by Ostrum and associates (case 5),[83] by Snyder and Hunter (case 2),[84] and by Steinberg.[81] When the aneurysm is of syphilitic etiology, it is generally evident radiologically.

Of considerable interest is case 1 of Jones and Langley.[51] In this case, a 12-year-old boy had a systolic thrill in the left 2nd and 3rd interspaces accompanied by a harsh systolic and a softer diastolic murmur. The blood pressure was 120/30. There were marked arterial pulsations in the neck. At autopsy there was an aneurysm of the right coronary sinus and a high ventricular septal defect. The aneurysm and cusp sagged

* Of considerable help in differential diagnosis is the fact that in the cases without shunts there is no pulmonary over-circulation.

downward through the septal defect accounting for the aortic insufficiency. There was also bacterial endocarditis on the margins of the septal defect. Also of interest was the presence of a tongue of fibrous tissue arising from the annulus fibrosus and running up to the transverse ridge on the aneurysm wall lying between the muscle of the right ventricle and the endothelial lining of the aneurysm. The question may be raised as to whether this case may possibly represent an example of the present syndrome of ventricular septal defect with aortic insufficiency.

*Marfan's Syndrome:* In Marfan's syndrome dilatation of the aortic ring together with stretching and sacculation of the aortic cusps may produce a profound degree of aortic regurgitation.[85,86] This may give rise to a to-and-fro murmur at the base.[86] Another cardiovascular abnormality that may occur in Marfan's syndrome is an aneurysm of the sinus(or sinuses) of Valsalva[81,86,87] and when associated with aortic incompetence may present a to-and-fro murmur at the base of the heart.[81,87] Dissecting aneurysm may also be encountered in this disease and aortic regurgitation may result either from the dissection itself or from the associated dilatation of the aortic ring.[86] Bicuspid aortic valve (with or without coarctation[86]) may occur in Marfan's syndrome and also cause aortic insufficiency.

The presence of other stigmata of Marfan's syndrome (ectopia lentis, arachnodactyly, dolichocephaly, etc.) usually permits the correct diagnosis to be made.

*Traumatic Rupture of Aortic Valve:*[80,88] The traumatic rupture of an aortic cusp or a linear tear of the aorta near the aortic valve attachment, either from a blow over the precordium or from extreme straining, results in the production of aortic regurgitation with accompanying murmur. This usually should not be confused with the present syndrome because of the history of trauma.

*Coarctation of the Aorta with Bicuspid Aortic Valve:* Coarctation of the aorta with bicuspid aortic valve[89] at times may be confused with the present syndrome. The systolic murmur is usually heard maximally at the base in coarctation, but the diastolic murmur due to the bicuspid aortic valve is heard along the left sternal border. Weak or absent femoral pulsations and the roentgen findings of coarctation will usually lead to the correct diagnosis.

### OTHER CAUSES OF TO-AND-FRO OR CONTINUOUS MURMURS

There are, of course, many other conditions which may result in to-and-fro or continuous murmurs.

Those with shunts such as complete anomalous venous return[90–95] and pulmonary arteriovenous fistula[96–98] are ordinarily not associated with a wide pulse pressure or left ventricular enlargement and should not be difficult to distinguish. Other rare combinations such as tetralogy of Fallot with left to right shunt and aortic insufficiency may offer diagnostic difficulties. Anomalous pulmonary artery arising from the aorta[57] can usually be distinguished by cardiac catheterization and angiocardiography. Pulmonary atresia[31,99] as well as stenosis of a branch of the pulmonary artery[100] produces neither a shunt nor a wide pulse pressure. Normal venous hum and arteriovenous aneurysm of an intercostal or internal mammary artery must also be considered.

Other causes of aortic insufficiency such as dissecting aneurysm, the aortic insufficiency accompanying some cases of hypertension and some cases of rheumatoid arthritis,[101] as well as chronic aortitis of unknown etiology,[102] can usually be differentiated by careful history and physical examination.

## Difficulties in Diagnosis

The precise preoperative or antemortem diagnosis of this syndrome at times may be difficult. The clinical features have already been described and while characteristic, are not pathognomonic, as other conditions may simulate this condition as indicated in the section on *Differential Diagnosis.*

Cardiac catheterization is helpful in indicating a left to right shunt at the level of the right ventricle. However, other conditions than a ventricular septal defect can produce increased oxygenation in the right ventricle. These include ruptured aneurysm of the sinus of Valsalva into the right ventricle and patent ductus

arteriosus or aortic septal defect with pulmonic valve insufficiency.

In the two latter conditions passage of the catheter from the pulmonary artery into the aorta will help distinguish these defects from the present syndrome. Another rare source of confusion is rupture of an aortic aneurysm into the pulmonary artery and the presence of pulmonic valve insufficiency.

A ruptured aneurysm of the sinus of Valsalva into the right ventricle plus a ventricular septal defect or a ventricular septal defect with a bicuspid aortic valve and aortic insufficiency cannot be differentiated by cardiac catheterization. Other combinations of lesions which may be difficult to distinguish by cardiac catheterization are those of ventricular septal defect plus a patent ductus, or ventricular septal defect plus an aortic septal defect.

Difficulties that are encountered in the precise localization by cardiac catheterization of left to right shunts near the pulmonary valve have been well documented.[39,57] The presence of a higher oxygen content in the pulmonary artery than in the right ventricle when the oxygen content in the right ventricle itself is greater than that in the right atrium, has been shown[39] to occur in the following conditions: (1) ventricular septal defect, presumably because of streamline flow in the outflow tract of the right ventricle and in the pulmonary artery; (2) aortopulmonary shunt associated with pulmonary valve insufficiency; and (3) aortopulmonary shunt associated with an interventricular defect. When this so-called "double gradient" in the oxygen content of mixed venous blood occurs, precise localization of the defect is difficult unless the catheter can be manipulated through the defect (or defects).

Such a double gradient was encountered in case 5 of our series in which only a presumptive diagnosis has been made. This double gradient was encountered in the case of Morgan and Burchell[55] which later proved to be an aneurysm of the sinus of Valsalva which had ruptured into the right ventricle associated with a ventricular septal defect.[56] In case 3 of Winchell and Bashour[24] there was an increase in the oxygen saturation only at the level of the pulmonary artery. At surgery no aorticopulmonary communication was demonstrated.

## Comment

Despite the long list of conditions that may simulate a ventricular septal defect with aortic insufficiency, the correct diagnosis is often possible by means of a careful history, physical examination, and certain laboratory aids. The following clinical features bear emphasis:

*History:* The murmur has been noted usually in infancy or childhood. There is ordinarily no history of rheumatic fever. Bacterial endocarditis is not rare in this condition. There has been usually no history of sudden occurrence of severe chest pain and usually no history of cyanosis. There is not infrequently a history of arrhythmia or congestive heart failure.

*Physical Examination:* There is a loud systolic murmur accompanied by a thrill usually maximal in the left 2nd to 4th interspaces adjacent to the sternum. A blowing diastolic murmur along the left sternal border is present. The murmur may at times be continuous and again is maximal to the left of the sternum. There are peripheral signs of aortic insufficiency. Central cyanosis and clubbing are absent. The heart is enlarged to the left and there is a left ventricular apical impulse. A mitral diastolic rumble is occasionally encountered.

*Roentgen Examination:* Chest films and fluoroscopy reveal predominantly left ventricular enlargement although occasionally the right ventricle may also be enlarged. The pulmonary arc segment is prominent. There is pulmonary over-circulation. The aorta is normal or slightly dilated and shows dynamic pulsations.

*Electrocardiogram:* The electrocardiogram usually shows left ventricular hypertrophy or combined hypertrophy. Some reported cases show right ventricular hypertrophy or right bundle branch block.

*Cardiac Catheterization:* Cardiac catheterization demonstrates an increased oxygenation at the right ventricular level. Occasionally this rise in oxygenation is observed in the pulmonary artery and in some instances the so-called "double gradient" is observed. There is often moderate pulmonary hypertension. Arterial oxygenation is normal although it is reasonable to believe that some cases with very high pulmonary vascular resistances may have some degree of right to left shunt.

*Angiocardiography:* Selective angiocardiography with the catheter in the right ventricle or pulmonary artery may show refilling of the right ventricle and pulmonary artery via the ventricular septal defect.[21]

*Aortography:* Thoracic aortography may rarely show regurgitation of contrast material into the left ventricle through the insufficient aortic valve with a left to right shunt of contrast material into the right ventricle. In other cases it may merely serve to exclude the presence of a patent ductus, aortic septal defect or ruptured aneurysm of the sinus of Valsalva.

*Dye Dilution Studies:* Theoretically, comparison of systemic arterial dye dilution curves obtained by injection of dye into the left ventricle, left atrium, and aorta might be of value in the differential diagnosis of this syndrome. However, to our knowledge, no such studies have yet been performed in this condition.[103]

Because of the possibility of surgical treatment of this anomaly, a correct preoperative diagnosis becomes mandatory. This is especially important if the technic of aortic occlusion, with or without cardiac arrest, is not used during the surgical procedure. Under these conditions the presence of aortic insufficiency would result in a large volume of blood being perfused through the aortic valve and into the ventricular chambers. There has been, at the time of this writing, only one reported attempt to repair the septal defect in this condition and it was unsuccessful.[27]

## Summary and Conclusions

During the past four years we have had the opportunity to observe seven cases of what we believe to be examples of ventricular septal defect with aortic insufficiency. The patients ranged in age from 5 to 37 years. The diagnosis was confirmed by autopsy in one case. In five the diagnosis was supported by cardiac catheterization, in one in addition by an angiocardiogram and a retrograde aortogram, and in one by exploratory thoracotomy.

There was usually a history of exertional dyspnea and frequently of congestive heart failure. The positive physical findings consisted of an enlarged heart, a loud systolic murmur most commonly heard maximally in the left 2nd to 4th interspaces, and a high-pitched diastolic murmur transmitted down the left sternal border. A continuous murmur was heard in one case. The pulse pressure was wide in all. Cardiac fluoroscopy revealed an enlarged heart with a prominent pulmonary arc segment, pulmonary over-circulation, and dynamic pulsations of the aorta. The electrocardiogram showed left ventricular hypertrophy in three cases, combined ventricular hypertrophy in three cases, and right bundle branch block in one.

Cardiac catheterization demonstrated pulmonary hypertension and an increase in oxygenation at the right ventricular level.

The previously reported cases of this syndrome are reviewed. There have been 22 cases with autopsy findings. In all cases proven by autopsy one or more of the aortic valve cusps were either thickened and deformed or unsupported, or both. In several of the cases the affected valve was described as being sacculated, ballooned, or even having an aneurysmal dilatation. Nine of the autopsied cases have had cardiac catheterization studies performed.

The differential diagnosis of this syndrome from other conditions with to-and-fro or continuous murmurs at the base of the heart plus a wide pulse pressure is discussed.

With the advent of surgical therapy for intracardiac and extracardiac lesions associated with left to right shunts, the correct diagnosis of this syndrome becomes mandatory.

## Addendum

Since the manuscript was accepted for publication, case 2 (P. K.) expired. At autopsy, findings characteristic of ventricular septal defect with aortic insufficiency were noted. The heart was huge, weighing 1,185 g. The left ventricle measured 17 mm in thickness and the right ventricle measured 13 mm in thickness. There was a defect in the membranous portion of the interventricular septum measuring 1.5 cm in diameter. The opening was reduced to a crescent shaped slit by the prolapsed left coronary artery cusp. There was aneurysmal dilatation of the cusp, measuring approximately 2.5 x 1 5 cm and it fit rather snugly into the septal defect. There was some thickening of the aortic valve leaflets.

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# Ventricular Septal Defect and Aortic Insufficiency

## Report of Three Cases*

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A RECENT report[1] has described a number of cases of ventricular septal defect in association with aortic insufficiency. Since this is an uncommon lesion,[2] the purpose of this paper is to document three similar cases, and again to emphasize the extreme difficulty in differentiating the condition from patent ductus arteriosus, a sinus of Valsalva aneurysm rupturing into the right ventricle or pulmonary artery, an aortic septal defect and several other uncommon lesions.

### CASE HISTORIES

CASE 1. This 18-year-old asymptomatic girl, with a murmur known since birth, had no history of cyanosis, scarlet fever, rheumatic fever, or any of its equivalents. Her family physician sent her to another hospital for investigation in 1954. A right heart catheterization was performed on January 15, 1954, and revealed the findings shown in Table I. These were interpreted as due to a patent ductus arteriosus, although an aortic septal defect was also mentioned. An aortogram was unsatisfactory. Surgery on January 19, 1954, revealed only a ligamentum arteriosum. A faint thrill over the first portion of the pulmonary artery and outflow tract of the right ventricle led to the conclusion that she had an aortic septal defect, but closure was not attempted.

*Clinical Findings:* On February 23, 1955, she came under our care. *Physical examination* revealed a thin, young, white female, without cyanosis. Blood pressure was 128/0. The apical rate was 88 and regular. The heart was not enlarged to percussion. There was a precordial continuous machinery murmur, with systolic accentuation and thrill, which was loudest in the second and third left intercostal spaces. The peripheral pulses were collapsing in type; there were no signs of cardiac failure.

*Radiologic studies* (Fig. 1) revealed a grade 2 to 3 enlargement of the heart, apparently affecting both ventricles equally, with a moderate prominence of the pulmonary artery segment and hilar vessels. An aortogram was not fully satisfactory but no abnormal communication was clearly demonstrated.

Fig. 1. Case 1. Chest x-ray (see text).

*The electrocardiogram* showed normal sinus rhythm, a semivertical electrical position, and left ventricular hypertrophy and strain.

*Operative Findings and Procedure:* Because of the report of the previous operation, it was decided to explore the patient for an aortic septal defect. On March 3, 1955, her chest was opened. The right ventricle was enlarged 2 plus, but the pulmonary artery appeared normal and no thrill was palpable over it. There was a harsh systolic and diastolic thrill over the root of the aorta and

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TABLE I
Cardiac Catheterization Studies

| Case | Sex-age | Oxygen content (Vol. %) | | | | | | | $O_2$ consumption (cc/min) | Systemic blood flow (l/min) | Pulmonary blood flow (l/min) | L-R shunt (l/min) | R-L shunt (l/min) | Overall shunt (l/min) | Pressures | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | SVC | IVC | RA | RV | MPA | LPA | RPA | FA or BA | | | | | | | RA | RV | PA | FA or BA | PVC |
| 1 | F-18 | 8.8 | 8.7 | 8.8 | 9.1<br>10.1<br>10.2 | 10.1 | 10.1 | 10.3 | 13.1 | ... | ... | ... | ... | ... | ... | ... | ...<br>50/8<br>34/9<br>40–52<br>10 | 39/17<br>33/17<br>46/17<br>35/14 | 142/42 | ... |
| 2 | M-29 | 13.9 | ... | 14.9<br>15.0 | 17.8<br>19.6<br>17.5<br>18.7 | 18.6 | 17.2 | 18.2 | 20.1<br>(saturation 91%) | 255.8 | 5.0 | 8.3 | 4.0 | 0.7 | 3.3<br>(L-R) | (5) | | | 154/76 | (15) |
| 3 | F-51 | 10.3 | ... | 11.3<br>11.1<br>10.6 | 11.7<br>12.5<br>14.1 | 13.2 | 14.2 | ... | 15.2<br>(saturation 87.5%) | 192.2 | 4.6 | 6.6 | 3.2 | 1.2 | 2.0<br>(L-R) | (10) | 48<br>13 | 40<br>18 | 90<br>35 | (20) |

SVC—Superior vena cava. IVC—Inferior vena cava. RA—Right atrium. RV—Right ventricle. MPA—Main pulmonary artery. LPA—Left pulmonary artery. RPA—Right pulmonary artery. FA—Femoral artery. BA—Brachial artery. PVC—Pulmonary venous capillary ("wedge"). L-R—Left to right. R-L—Right to left.

the anterior surface of the right ventricle. No ventricular septal defect or infundibular ridge was encountered by a urethral sound used to probe the outflow tract of the right ventricle. The only correctible lesion seemed to be aortic insufficiency, and accordingly a heavy nylon ligature was threaded around the aortic annulus, as described by Bailey.[3] At the completion of the procedure, the diastolic thrill at the root of the aorta was much decreased, but the systolic thrill over the right ventricle remained very prominent.

*Postoperatively*, her blood pressure was 100/40–0. On the tenth postoperative day, after several days of complete heart block with multiple ventricular premature beats, sudden asystole supervened, and cardiac action could not be restored.

*Autopsy Findings:* At postmortem examination, a high interventricular defect was found (Fig. 2), the upper



Fig. 2. Case 1. Autopsy. Left ventricle cut open, showing septal defect and section of nylon ligature placed around aortic annulus.

margin being formed by the aortic annulus and the inferior surface of the right aortic cusp. The aortic cusps were all thin, flexible, and without commissural fusion. In the cadaver, there was no evidence of aortic insufficiency. The nylon ligature was properly placed about the annulus, and the coronary vessels were not constricted in any way. Except for congestion, all other organs were normal.

CASE 2. A 29-year-old white German male was told sometime in his childhood that he had been born with

heart disease. However, his activities were not limited. Cyanosis was never observed and he never had rheumatic fever. During the 1940's he was a refugee and underwent considerable hardship, without symptomatology. On coming to this country in 1953, he was told by a well-known cardiac surgeon that he did not have a correctible lesion. He remained largely asymptomatic, although systemic review did reveal palpitation for ten years and fatigue for five years. About five weeks prior to admission in April 1955, on receiving unexpected tragic personal news, he had an episode of syncope. This prompted him to have further investigation of his cardiac status.

*Clinical Findings: Physical examination* revealed a husky young white male, with a blood pressure of 116/54/40 and an apical rate of 88 that was basically regular, interrupted by premature systoles. The heart was not enlarged to percussion. There was a very loud grade 4 harsh continuous murmur over the precordium, loudest in the fourth and fifth interspaces near the left sternal border. In this location, there was also a systolic and diastolic thrill. The first and second heart sounds at the apex and base were obliterated by the murmurs.

*X-ray and fluoroscopic study* (Fig. 3) showed a grade 1

Fig. 3. Case 2. Chest x-ray (see text).

to 2 cardiac enlargement, involving the right and left ventricles, mostly the latter, and also to a slight extent the pulmonary artery segment and hilar vessels. The hilar pulsations were only slightly increased.

*The electrocardiogram* showed normal sinus rhythm with premature ventricular contractions, a normal electrical axis and position. The sum of S in $V_2$ and R in $V_5$ was 60 mm, but there was no "strain" pattern.

*The cardiac catheterization findings* are seen in Table I. They demonstrate a left to right shunt at the ventricular level of 4.0 *l*/min, a right to left shunt of 0.7 *l*/min, minimal pulmonary hypertension, and a widened peripheral pulse pressure.

In view of the minimal symptomatology and slight increase in heart size, surgery was not advised. No follow-up is available.

CASE 3. This 51-year-old white female first learned of a heart murmur at the age of 17, during a routine examination. There was no history of rheumatic fever or any of its equivalents. She was asymptomatic during two pregnancies (ages 25 and 29). About 1948, following a tooth extraction, she developed subacute bacterial endocarditis and was treated with dicumarol and penicillin for some weeks. She recovered and was again without symptoms until the fall of 1955, when the diagnosis of bacterial endocarditis was again made by blood culture, and the patient was treated with 20 million units of penicillin daily for 30 days, with complete recovery.

Systemic review was noncontributory, except for slight exertional dyspnea in the year before admission, and mild palpitation for 4 months. Other cardiac symptoms were denied.

*Clinical Findings: Physical examination* revealed a blood pressure of 190/90 initially; later readings were about 106/60. The apical rate was 80 and regular. The heart was enlarged to percussion. There was a grade 3 harsh systolic and grade 2 to 3 early blowing diastolic murmur over the precordium, loudest in the third interspace near the left sternal border, and almost continuous in character. The aortic and pulmonic second sounds were absent. There were no peripheral signs of aortic insufficiency. The lungs were clear, the liver was not enlarged, and there was no edema or cyanosis.

*On roentgenologic study* (Fig. 4), there was noted a grade 3 cardiac enlargement, involving both ventricles, and a grade 2 enlargement of the pulmonary artery segment and pulmonary vessels. The hilar pulsations were moderately increased.

*The electrocardiogram* showed normal sinus rhythm, a normal electrical axis and position, and no evidence of ventricular hypertrophy.

*Cardiac catheterization* revealed the highest oxygen content on the right side of the heart to be in the outflow tract of the right ventricle (see Table I), with minimal pulmonary hypertension, slight systemic arterial oxygen unsaturation, and a low systemic diastolic pressure. The calculated left to right shunt was 3.2 *l*/min, the right to left shunt 1.2 *l*/min.

*An aortogram* yielded very satisfactory filling of the aorta and early filling of the pulmonary vascular tree, apparently through a connection at the root of the aorta (see Fig. 5).

*Operative Findings and Procedure:* It was decided to perform surgery for the correction of an aortic septal defect. At operation on March 12, 1956, no such defect was found, nor was there any patent ductus arteriosus. In the outflow tract of the right ventricle,

an opening was felt, high in the septum, about 2 cm in diameter. The septal cusp of the aortic valve bulged into the defect and appeared deformed due to lack of support in this region; a regurgitant jet of blood could be palpated in the left ventricle. Because the outflow tract of the right ventricle was large, it was elected to invaginate this into the defect and sew it with silk sutures around the margins of the defect in the manner described by Bailey *et al.*[4] for closure of an atrial septal defect. At the end of the operation, the diastolic thrill and the major part of the systolic thrill had been abolished, leaving only a faint systolic thrill over the outflow tract of the right ventricle.

*Postoperative Course:* On the 13th postoperative day another cardiac catheterization was performed. It showed no evidence of a right to left or left to right shunt. However, the right ventricular pressure was 60/10 and the pulmonary artery pressure 28/16, while the corresponding pressures prior to surgery were 48/12 and 40/18, indicating that a moderate obstruction had been created in the outflow tract of the right ventricle.

After catheterization she was febrile, and after several days blood cultures revealed a coagulase-negative staphylococcal bacteremia. She was treated with oxytetracycline and streptomycin, and eventually recovered. During this time, her systolic murmur, which was believed to have been caused by the surgically created obstruction in the right ventricular outflow tract, was replaced by the original systolic and early diastolic murmurs. Apparently, she developed bacterial endocarditis and, either as a result or concomitantly, the septal defect reopened and aortic insufficiency was reestablished, as the septal aortic cusp lost the support produced by surgical closure of the defect. (A third catheterization was not performed.)

## Discussion

These three cases, apart from the interesting surgical implications of the third, present clearly the difficulty involved in differentiating the combination of ventricular septal defect and aortic insufficiency from several other lesions, especially the more commonly seen patent ductus arteriosus. Perhaps this combination ought to be considered more often in the differential diagnosis of the latter lesion. Usually, an aortic septal defect is mentioned first in the differential diagnosis of patent ductus, but Gasul *et al.*,[5] in 1951, found only 24 reported cases of aortic septal defect in all the literature, while Gross,[2] in 1952, reported 12 cases of ventricular septal defect and aortic insufficiency in one series of 525 cases of patent ductus arteriosus.

Actually, this differential diagnosis must also include aneurysm of the sinus of Valsalva communicating with the pulmonary artery or right ventricle,[6] any left to right intracardiac shunt with pulmonary hypertension and pulmonic valve insufficiency, coronary arteriovenous fistula, any arteriovenous fistula of systemic vessels in the chest near the heart, and an anoma-

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Fig. 4. Case 3. Chest x-ray (see text). Fig. 5. Case 3. Aortogram showing Diodrast escaping from aorta anteriorly (A), filling pulmonary artery early (B).

lous coronary artery communicating with a ventricular chamber.[7]

THE HISTORY IN DIFFERENTIAL DIAGNOSIS

Such a differential diagnosis on clinical grounds is nearly impossible. The history is of little help. Since all these cases involve some congenital defect, they may all have a history of a murmur present from very early in life. The murmur may not have the same character early in life, but this fact is not usually known to the patient. A patient with a ventricular septal defect or atrial septal defect may have only a systolic murmur at first, and not develop a diastolic murmur until later in life, after pulmonary hypertension and pulmonary valve insufficiency have appeared. This group of patients may develop cyanosis after the pulmonary pressure has increased enough to cause a right to left shunt, but this may also occur with a patent ductus arteriosus, late in the course of the disease. At such a time, the typical continuous murmur of the ductus may be markedly altered. Otherwise, in none of these conditions will there be a history of cyanosis.

The presence or absence of heart failure in the history is not helpful, since it may occur in all, and depends on the magnitude of the shunt or valvular insufficiency rather than on the character of the lesion. In the case of a ruptured sinus aneurysm, if the rupture occurs as a sudden event sometime in adult life, heart failure may appear quickly and lead to death over a period of months to years. On the other hand, the communication between the aneurysm and the right side of the heart may be congenital and heart failure may never appear, or do so gradually. Jones and Langley's[8] excellent article discusses the statistics available on such cases.

Bacterial endocarditis or endarteritis may appear in any of these lesions, so that it is not helpful in the differential diagnosis. The anginal syndrome has not been reported to our knowledge in any of these various lesions, although one might speculate that it could occur in coronary arteriovenous fistula or with a ruptured sinus aneurysm or with aortic insufficiency (and a ventricular septal defect). Other possible cardiac symptoms, such as syncope, cough, hemoptysis, and palpitation, have not been prominent in the history of any of these conditions.

PHYSICAL EXAMINATION

The physical examination is not a great deal more helpful in the differential diagnosis of these lesions. The *blood pressure*, and especially the diastolic pressure and pulse pressure, are not characteristic. The wide pulse pressure and low diastolic pressure may occur wherever there is a large run-off from a high pressure to a low pressure system—in aortic insufficiency, a large patent ductus arteriosus (but not after pulmonary hypertension and pulmonary valvular insufficiency have appeared), a ruptured sinus aneurysm, and an aortic septal defect. A wide pulse pressure also could be seen with a large systemic arteriovenous fistula. It would not occur in cases of left to right intracardiac shunts, with pulmonary hypertension and pulmonary valve insufficiency, nor in cases of a coronary artery communicating with a ventricular chamber.

The physical signs of *cardiac enlargement*, both as to location and character of the cardiac impulse, are of no value. The same is true with respect to the signs of congestive heart failure. The presence or absence of cyanosis on physical examination has no more significance than discussed in the history.

*Auscultatory Signs:* The cardiac auscultatory signs may be of some help. In general, the aortic second sound is likely to be normal, even in the case with aortic insufficiency and ventricular septal defect, since the valve leaflets are not markedly diseased. The pulmonic second sound is usually intensified, although not necessarily so in the cases of systemic arteriovenous fistulae (including those of the coronary vessels); it is usually very loud in patients with a left to right shunt, especially after the development of pulmonary hypertension.

The murmurs themselves are often confusing, and this indeed is the reason for discussing these various lesions in one paper. It certainly is not of much clinical value to say that the point of maximum intensity of the murmur of a ruptured sinus aneurysm or an aortic septal defect tends to occur further down along the left sternal border than the murmur of a patent ductus

arteriosus. Nor does it help to say that the diastolic murmur of aortic insufficiency is different in character or duration from the diastolic phase of a ductus murmur, particularly that it does not extend all the way through diastole. This was true in case 3, but not in cases 1 or 2. For practical purposes, the similarities are more confusing than the dissimilarities are helpful. Certainly only a bizarre location for a murmur—well removed from the cardiac area—would be useful in suggesting the presence of a systemic arteriovenous fistula within the thoracic cage. The murmur of a pulmonary arteriovenous fistula would vary with respiration, and would be associated with unsaturation of systemic arterial blood, if not visible cyanosis.

ECG FINDINGS

The electrocardiogram may offer some helpful clues, although the degree of abnormality may be minimal. There is a tendency to right ventricular preponderance in cases of left to right shunt with pulmonary hypertension or in cases of ruptured sinus aneurysm. Aortic septal defect or patent ductus, uncomplicated, tends to show left ventricular preponderance, and this is true of a systemic thoracic arteriovenous fistula if it is large enough. On the other hand, a coronary arteriovenous fistula might show the electrocardiographic changes of coronary insufficiency. Where a ventricular septal defect and aortic insufficiency coexist, there may be a tendency for the two lesions to balance out their effects electrocardiographically, giving rise to no specific abnormal pattern (case 3). The finding of an arrhythmia is not diagnostic; most of the patients have normal sinus rhythm, a few may have atrial fibrillation, but this is probably more the result of duration of the disease and degree of myocardial disability than of a specific lesion.

CATHETERIZATION FINDINGS

Physiologic studies with a cardiac catheter may locate a left to right shunt at atrial, ventricular, or pulmonary artery level. The catheter may pass through a patent ductus arteriosus or through an aortic septal defect from the pulmonary artery to the aorta. In the left anterior oblique or left lateral view, one might expect a catheter to pass more anteriorly when an aortic septal defect is present, and to enter the aorta more posteriorly when the lesion is a patent ductus arteriosus. However, Figures 6 and 7 are from two surgically confirmed cases of

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Fig. 6. Catheter passing from pulmonary artery into aorta in case of patent ductus arteriosus. Note how far anteriorly the catheter is seen. Fig. 7. Catheter passing from pulmonary artery into aorta in another case of patent ductus arteriosus. Note that the catheter is more posteriorly located before it passes into aorta.

patent ductus arteriosus, despite the apparent difference in the position of the catheter where it seems to enter the aorta. Moreover, occasionally, with a shunt above the pulmonary valve, the first sample showing a high oxygen content may be obtained just below the valve, making one suspect a ventricular septal defect when such is not present. Even if the shunt is truly in the right ventricle, it may be coming from the aorta through a ruptured sinus aneurysm, or from the aorta via a high ventricular septal defect and an incompetent aortic valve leaflet.

A coronary artery communicating directly with the right ventricle might show a small left to right shunt in the ventricle, but its source could not be determined. A coronary or internal mammary (or other intrathoracic systemic) arteriovenous aneurysm could likewise not be determined by catheterization. Perhaps if a sample were obtained from the coronary sinus and found to be unusually high in oxygen content, such a communication in the coronary system could be suspected in the presence of the characteristic murmur, although one could not exclude anomalous pulmonary venous drainage into the coronary sinus, with some other lesion to explain the double murmur.

*Pulmonary Hypertension:* In cases with a communication between the right and left side of the heart, when pulmonary hypertension develops sufficient to produce pulmonary valvular insufficiency and a diastolic murmur, the systolic murmur may disappear. If it remains, so that one of the other lesions we are discussing must be considered in the differential diagnosis, the catheterization will be of help if a systemic arterial blood sample obtained during the procedure shows unsaturation, since this would not be seen in uncomplicated patent ductus arteriosus, ruptured aortic sinus aneurysm, ventricular septal defect with aortic insufficiency, coronary arteriovenous aneurysm or coronary artery-ventricular communication. However, the presence of pulmonary hypertension, although it can be detected by catheterization, is of no help by itself in differentiating these lesions. All of them may result in pulmonary hypertension, at least theoretically (except coronary arteriovenous aneurysm), but none of them must necessarily do so; perhaps a ventricular septal defect is most likely to do so, but in any one case this finding would be of little help.

### RADIOLOGIC FINDINGS

X-ray and some of the more recent radiologic technics with Diodrast® may be helpful in establishing the diagnosis. Patent ductus arteriosus, aortic septal defect, and ventricular septal defect with aortic insufficiency all may show cardiac enlargement involving primarily the left ventricle (although the latter two may also show right ventricular enlargement), with prominence of the pulmonary vascular markings and the pulmonary artery segment. The degree of expansile aortic pulsation is a reflection of the width of the pulse pressure and is no more helpful than the latter in the differential diagnosis. The pulmonary vascular pulsation is likewise a reflection of the volume of the left to right shunt, and, therefore, not helpful. A large aortic sinus aneurysm may be diagnosed by x-ray, but the type of sinus aneurysm which ruptures into the right ventricle or pulmonary artery is usually congenital and small and, hence, not visible on x-ray. Once a communication between right and left halves of the circulation has given rise to bidirectional shunting and pulmonary hypertension, the x-ray picture can not differentiate at what level the communication is present.

*Selective Angiocardiography:* With the injection of diodrast into the appropriate chamber, it may be possible to visualize the actual location of shunts in either direction by knowing the order in which the chambers normally should be opacified and by observing the order in which they actually are rendered opaque. It is quite possible to introduce a needle into the left atrium now. Although Zinsser[9] was able to visualize this chamber well by ordinary venous angiography in a study of mitral stenosis, an atrial defect surely could be visualized better by injecting the diodrast into the left atrium. The same is true of dye injected into the left ventricle to demonstrate passage of the circulatory stream directly into the right ventricle. Much depends on the rapidity with which a bolus can be made to enter the desired chamber, and on the rapidity with which films can be taken, but with proper equipment this should be a very useful diagnostic

method, especially where the shunt is small and not picked up by cardiac catheterization.

*Aortography:* Finally, an aortogram can be performed to demonstrate a shunt into the pulmonary artery, although it is possible that no differentiation could be made with certainty between an aortic septal defect and a ruptured sinus of Valsalva aneurysm into the pulmonary artery. Even the demonstration of dye in the right ventricle following an aortogram would not prove that rupture of a sinus had occurred, because aortic insufficiency and a ventricular septal defect could cause dye to enter the right ventricle from the aorta without necessarily showing dye in the left ventricle. This can happen because the orifice of the aorta is so close to a high ventricular septal defect that dye could pass directly through it without entering the main portion of the left ventricle.

In connection with diodrast injection, the development of more rapid film-changing apparatus or the use of cineradiography with image intensifiers may make more practical these attempts to demonstrate the location of the anatomic defects under consideration. In any event, it seems likely that a combination of all possible diagnostic means will be necessary to ascertain the actual lesion(s) present in any given case. Even then, a combination of lesions may confuse the picture and make an autopsy the only method of defining the anomalies.[10,11]

## Summary

(1) Three case reports of probable ventricular septal defect with aortic insufficiency are reported. One was misdiagnosed clinically and discovered at autopsy. The second was diagnosed by clinical means with the aid of cardiac catheterization. The third was diagnosed in a like fashion, with the aid of an aortogram, and proved at surgery (at which time the septal defect was closed, with the production of a moderate infundibular pulmonary stenosis).

(2) A discussion of the various differential diagnostic possibilities includes: the lesion described in the case reports, aortic septal defect, patent ductus arteriosus (with or without pulmonary hypertension and pulmonary valvular insufficiency), atrial or ventricular septal defect with pulmonary hypertension and pulmonary valvular insufficiency, sinus of Valsalva aneurysm with rupture into the right ventricle or pulmonary artery, coronary arteriovenous fistula, arteriovenous fistula of any thoracic systemic vessel near the heart, and anomalous coronary artery communicating with a ventricular chamber.

(3) The differential diagnosis can seldom be made on the basis of the physical findings or the history. The electrocardiogram offers some help in excluding the septal defects with pulmonary hypertension, because right ventricular hypertrophy will be present in these circumstances. The cardiac catheterization and the x-ray findings, particularly when proper use is made of injected diodrast, offer the greatest help in making the proper diagnosis.

## Acknowledgment

All of the catheterization and other physiologic data were supplied by Dr. Harry Goldberg, Director, Brith Sholom Cardiopulmonary Laboratory of Hahnemann Medical College and Hospital of Philadelphia.

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# Significant Cardiac Arrhythmias Induced by Common Respiratory Maneuvers*

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THE ROLE of the carotid sinus reflex in slowing the heart and in causing cardiac arrest in certain instances is well known. Not so well known is the role of respiratory reflexes in relation to cardiac arrhythmias. Not only may such reflexes be associated with cardiac slowing but it was surprising to discover that they were capable of precipitating serious cardiac arrhythmias. Some of the arrhythmias seen to date in association with common respiratory maneuvers are: sinus arrest with ventricular escape, A-V block, ventricular premature beats, ventricular bigeminy, atrial bigeminy, paroxysmal nodal tachycardia, changes in the order of ventricular excitation in complete right and left bundle branch block, conversion of typical WPW conduction to normal conduction, and precipitation of WPW conduction in the presence of normal conduction. The occurrence of a cardiac arrhythmia in a pilot may well have been responsible for an aircraft accident which resulted in the death of a young flight surgeon. The purpose of this report is to point out some of the important arrhythmias noted, their general clinical significance and to recommend certain precautions to avoid a serious change in cardiovascular hemodynamics in individuals in such sensitive occupations as aviation.

## OBSERVATIONS

*Cardiac Slowing During Breath-Holding:* The most common response to respiration may be demonstrated in most subjects by having them take a deep breath and hold it at the height of maximum inspiration. At that particular point there is usually significant slowing of the cardiac rate (Fig. 1). A previous rate of 80/min may fall to a cycle length of 30/min. This response is best elicited in the recumbent position although it may also be present while standing. There appears to be a marked variability from one individual to the next in response to this maneuver. The point at which the breath is held appears to be the trigger point. Following a peak response the rate begins to return to normal or preinspiratory levels. This response is entirely normal and has not been shown to have any adverse effects on the circulatory dynamics. It is comparable to the usual carotid sinus reflex slowing seen in normal subjects.

These findings are consistent with previously reported effects of respiration on cardiac rate.

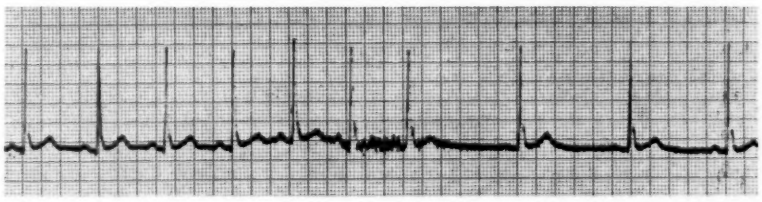

Fig. 1. An example of marked slowing in a normal subject taking a deep breath and holding it. Tremor occurs at, the height of inspiration and may be seen on the record.

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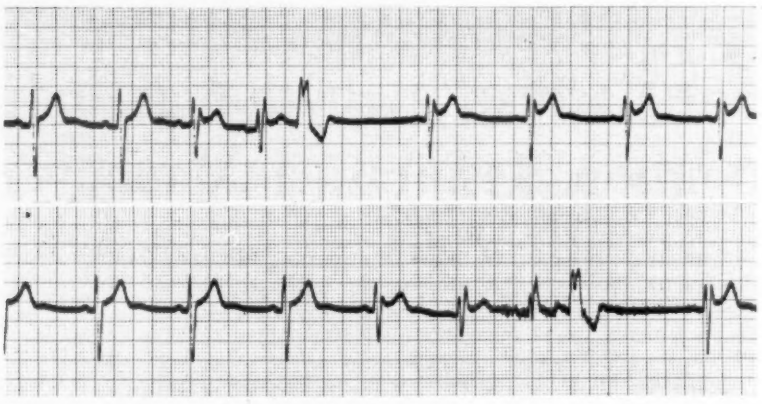


Fig. 2. An example of ventricular premature beats occurring at the height of inspiration on two occasions.

It has been reported that a vagal reflex can be initiated by stimulating stretch receptors in the visceral pleura or the lung tissue immediately subadjacent to it.[1] The receptors apparently adapt readily. Normal inspiration ordinarily accelerates the heart. Prolonged normal inflation often causes secondary slowing of cardiac rate. With hyper-inflation cardiac slowing occurs, or the effect herein reported of reflex slowing of the heart at the height of inspiration occurs. This reflex has been described as being initiated through vagal afferent fibers and carried out through vagal efferent fibers. It is of further interest that the inhibitory phase has been reported to cause further abnormality in A-V conduction when a previous defect was present.

Early in our observations one of us (LEL), while performing the maneuver, had an episode of transitory cardiac arrest with ventricular escape.[2] This appears to be a relatively infrequent occurrence. This was also the phase of respiration in which one episode of transitory A-V block without ventricular response was noted in another subject. This maneuver causing conversion of WPW conduction to normal conduction has been observed. Changes in conduction in right and left bundle branch block has also been noted in this laboratory.

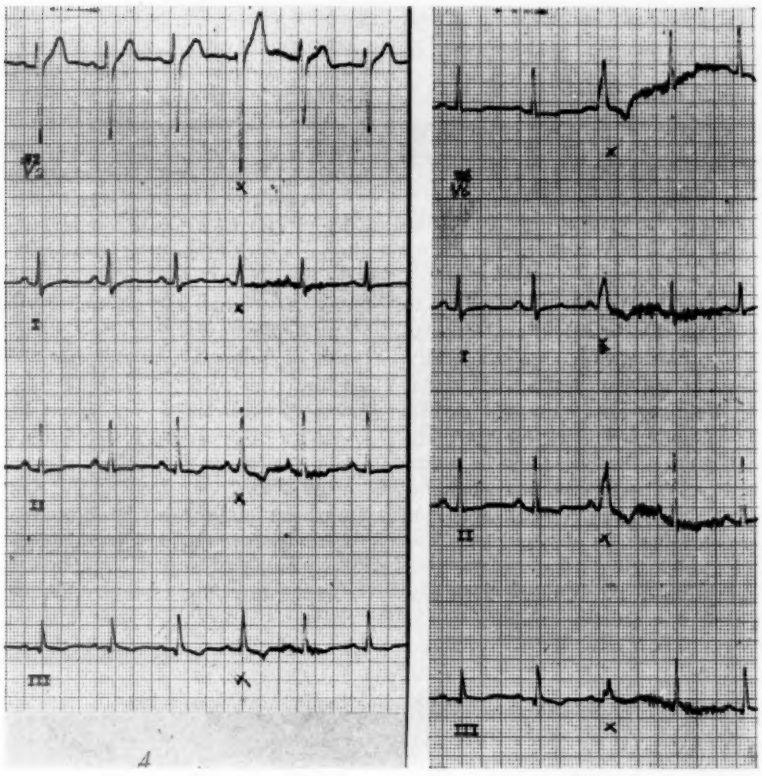
*Premature Beats and WPW Conduction on Deep Inspiration:* It is not uncommon to observe ventricular premature systoles at the height of inspiration in subjects with no other evidence of cardiac arrhythmia (Fig. 2). This may be regularly repeated in certain individuals. Such prematurities are not escape mechanisms associated with cardiac slowing but true premature systoles initiated by a focus other than the SA node. In one subject the ventricular focus resulted in various ventricular fusion beats which resemble. WPW complexes.

Case 1. G. U. was a 38-year-old man who complained of vague chest discomfort not associated with exertion. He had noted symptoms of palpitation with disturbance in heart beat with these episodes. On interrogation he gave a history of infrequent cardiac arrhythmia (irregular thumping) since 30 years of age. The only significant finding was an abnormal ECG (Fig. 3). Exercise tolerance studies* were performed and the electrocardiogram was recorded in the inspiratory and expiratory phase with persistent abnormality being demonstrated. The ST segment and T wave changes associated with the QRS findings raised the possibility of coronary artery disease as the basis of his chest discomfort. Subsequent evaluation failed to disclose a significant history of coronary insufficiency.

On deep inspiration WPW-like complexes were repeatedly produced. Due to their variability they were thought to represent ventricular fusion beats resulting from ventricular excitation from the usual SA node impulse passing over the atria and a second impulse arising from the ventricle. However, the history of cardiac arrhythmia at a young age without true anginal history and the ST segment and T wave changes suggested the possibility that this might be an atypical WPW syndrome with a variation in the usual order of ventricular excitation with secondary ST segment and T wave changes.

The conversion of normal conduction to WPW conduction in a known case of WPW syndrome has been previously reported,[3] and extreme variability of WPW complexes in known examples of WPW syndromes has

* Exercise tolerance tests are not normally done in the presence of an abnormal resting tracing particularly if the abnormality is thought to be due to coronary artery disease.



A B

Fig. 3. Case 1. Two different instances (A and B) of ventricular fusion beats resembling WPW conduction or aberrant ventricular conduction induced by deep inspiration.

been noted.[4] The respiratory maneuver in this case either disclosed an underlying WPW syndrome or caused ventricular fusion beats by precipitating discharge from a ventricular focus. The latter interpretation is more likely.

*Arrhythmias During Release of Breath:* Another point of initiation of cardiac arrhythmia occurs with release of breath after prolonged inspiration. Frequently ventricular premature beats are noted at this point. On some occasions when the cardiac rate has increased with holding the breath, cardiac slowing and marked sinus arrhythmia follows release of inspiration.

Case 2. J. K. was a 24-year-old officer who was asymptomatic. He acted as a control subject in experimental proceedings used in evaluating syncope. During the early phase of breath holding sinus tachycardia of 100/min was noted. Later, still holding his breath, the cardiac rate began to slow to 65/min. At the end of holding inspiration ventricular premature beats began. After release of inspiration with re-established normal respiration, ventricular bigeminy persisted for over two minutes (Fig. 4). Ventricular bigeminy recurred at the onset of hyperventilation and during recovery from hyperventilation. After the procedures were completed there was no evidence of ventricular premature beats.

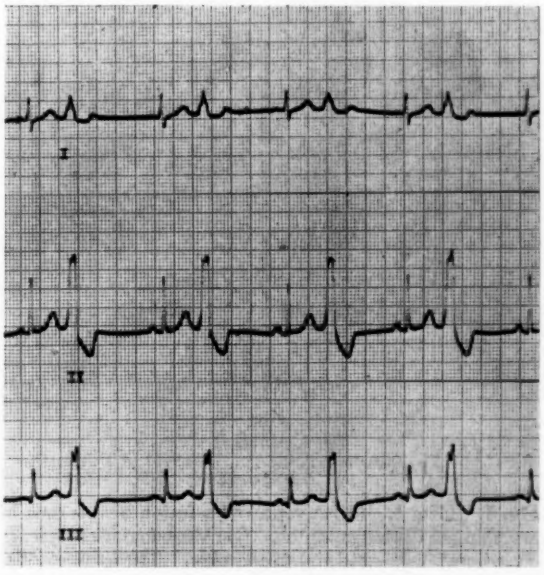


Fig. 4. Case 2. An example of ventricular bigeminy induced by breath holding.

None had been noted previously and none have been noted since.

*Effects of Hyperventilation:* Significant arrhythmias may also occur following hyperventilation. Our observations indicate that by taking a deep breath and holding it at the end of hyperventilation, arrhythmias may be precipitated in susceptible individuals.

Case 3. R. C. was a 25-year-old officer who was found to have what appeared to be episodes of ventricular premature systoles, occurring as a simple bigeminy. He was asymptomatic. Subsequent electrocardiographic studies identified an interesting and unusual cardiac arrhythmia (Fig. 5). The ventricular premature systoles originated from a parasystolic focus as evidenced by their inconstant coupling. The P wave was sometimes lost in the ventricular systole and at other times part of it could be identified preceding the QRS complex. Occasionally the impulse originating from the SA node and the impulse originating in the ventricle both took part in ventricular excitation causing varying forms of ventricular fusion beats. The marked differences in successive complexes probably represent changes in the order of ventricular excitation due to variations of ventricular fusion. The resting rhythm then was a very complex arrhythmia.

While investigating the behavior of the rhythm the patient was instructed to hyperventilate, then hold his breath. With breath held, transitory A-V dissociation with apparent nodal tachycardia ensued (Fig. 6). Aside from its relation to respiration this constitutes a real collector's item in cardiac arrhythmias. One might raise the question of ventricular tachycardia with incomplete A-V dissociation and successive ventricular fusion beats causing the appearance of nodal tachycardia. The presence of apparent P waves in the ST segment is evidence against this point of view. As the nodal tachycardia slowed, a ventricular impulse terminated the arrhythmia with an obvious ventricular fusion beat. The parasystolic premature systoles are of such a nature that they could arise from a focus in the right bundle. With an apparent nodal focus precipitating nodal tachycardia and a focus in the right bundle one might well ask if the parasystolic focus is wandering in its location, further complicating the identification of ventricular fusion beats. Another finding of some interest following the burst of nodal tachycardia is the paired ventricular im-

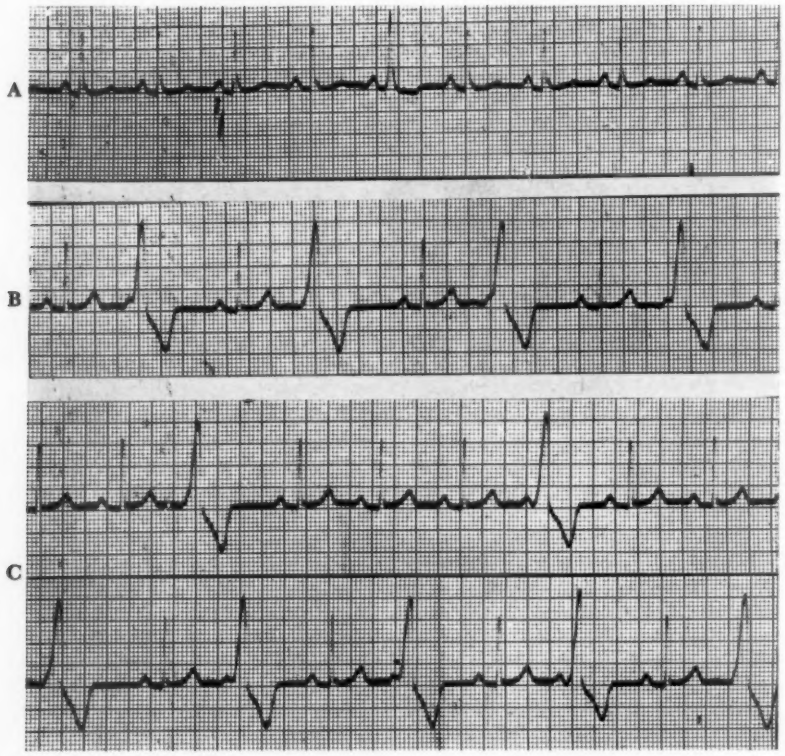



Fig. 5. Case 3. (A) A ventricular fusion beat is seen in the fifth systole. The ST segment and T waves show secondary changes in that complex. (B) Ventricular complexes are seen with upright P waves appearing at their onset in the second, sixth, and eighth complex. The inconstant relation of the ventricular ectopic impulse to the preceding complex is a characteristic of parasystole. (C) Another illustration of the inconstant relation of the ventricular impulse to the preceding complex.

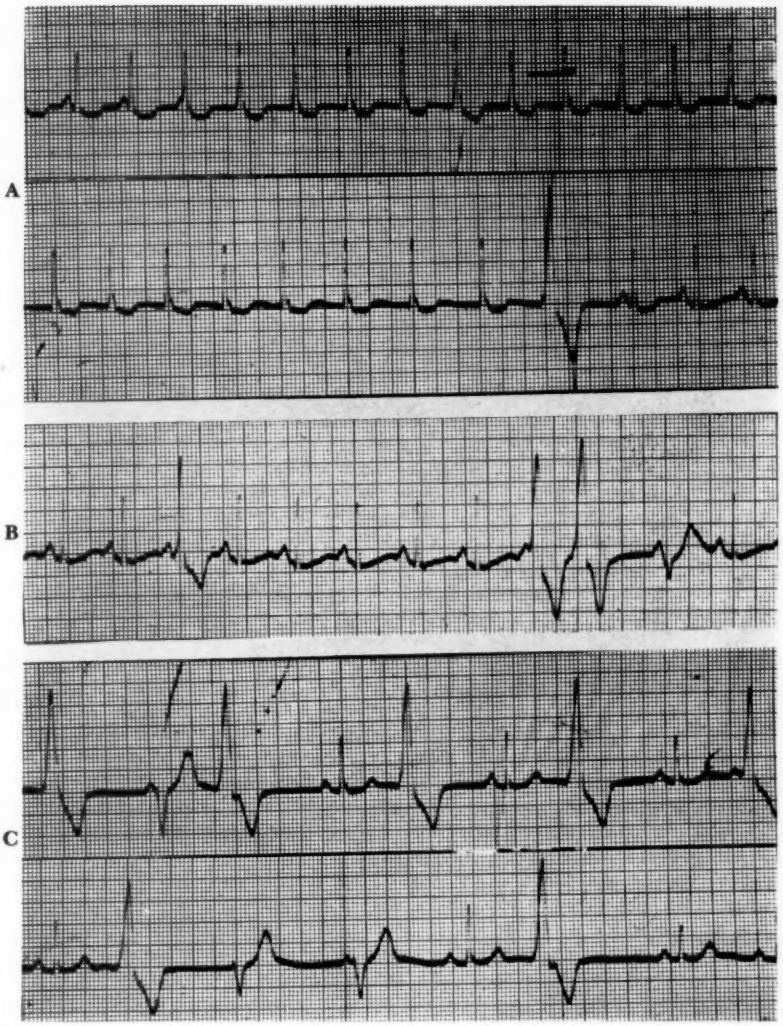



Fig. 6. Same patient as in Figure 5. (A) An episode of nodal tachycardia with A-V dissociation following hyperventilation and breath holding. Note that the P wave moves into the QRS complex. A P wave is visible in the ST segment of the sixth complex. As the ventricular rate slows the parasystolic focus discharges and normal sinus rhythm is restored. (B) Just after the episode of nodal tachycardia paired ventricular beats occur. (C) Further complications in ventricular excitation are indicated by the multiplicity of ventricular forms noted.

pulses suggesting an open door to the onset of ventricular tachycardia.

*Arrhythmias in Pilots:* Cardiac arrhythmias are of particular importance to aviation as some of them may significantly alter cardiovascular hemodynamics to the point of causing a syncopal episode. Obviously a pilot must not have syncope while in primary control of the aircraft. Individuals who are susceptible to significant arrhythmias should be detected as certain respiratory maneuvers with flying may stimulate the pulmonary reflexes mentioned, with disastrous consequence. The following case is believed to illustrate an unfortunate occurrence of such an arrhythmia resulting in an expensive aircraft accident and the death of a young flight surgeon who was a passenger on the flight.

Case 4. W. F. was a 32-year-old pilot in apparent good health. On December 21, 1956, he took off with his passenger, a flight surgeon, in a T-33 aircraft and flew to Omaha, Nebraska. He remained at Omaha for two to three hours and he and his physician passenger took off at 2:00 P.M. Los Angeles time. They climbed to 39,000 ft (cabin altitude 27,000 ft) and the pilot remembers having some difficulty exhaling into

his oxygen mask. The pilot remembers conversing with his passenger and then recalls nothing until he suddenly became aware that his airplane was "winding up" "making a lot of noise." He was unaware how this had occurred but realized that the aircraft was near the critical Mach number. His vision was hazy and he was unable to see the air speed indicator or read the altimeter. He attempted to reach for the throttle and the stick but was unable to do so because of the G forces. He recalls his passenger's asking, "Are you all right now?" He could not recall his answer but decided to abandon the aircraft, since he could not fly it and did not know the aircraft's altitude. He informed his passenger of his decision but received no answer. Not knowing the condition of his passenger he decided to continue to fly the aircraft. This proved to be impossible and he again announced to his passenger that they must abandon the aircraft. There was no response. Due to the G forces he was unable to reach the canopy release with his right arm alone and had to use both his left and right arms. The canopy blew off and he told his passenger to bail out. Since he was unable to determine what his passenger was doing he again attempted to fly the aircraft. This was unsuccessful and he decided to eject. The next thing he recalls is that he was in the air with his seat beside him. He pushed the seat aside with his left arm and pulled the D ring of his parachute. About this time he became fully aware of what was going on and looked up to see the chute lines shrouded. His chute opened and as he descended he was able to see the light on the ground and the aircraft crash. He recalls that there was an overcast reported between 2,500 and 3,000 ft and therefore he assumes that he was below this since he could see lights on the ground and the crash. Approximately 20–30 sec later the patient landed in a muddy field without difficulty except for a slight pain in his left chest. He climbed a number of fences to a farmhouse, called a nearby Air Force Base, and was picked up by ambulance and hospitalized. Other than a diagnosis of a "torn cartilage" no other abnormalities were found and the patient remained asymptomatic.

The flight surgeon who accompanied the pilot on the trip had ejected but failed to release his seat belt prior to releasing his D ring for his parachute. He was found dead near the scene of the aircraft accident. An exhaustive evaluation of the pilot indicated no abnormalities other than those associated with cardiac rhythm. On taking a deep breath and holding it the pilot developed lower nodal rhythm, rate 35/min, associated with loss of consciousness (Fig. 7).

Although it cannot be definitely established that a cardiac arrhythmia resulted in a syncopal episode associated with an aircraft accident, one cannot help but be suspicious in view of the history of difficulty in exhaling, a sudden gap in consciousness, and a subsequent demonstration of a significant cardiac arrhythmia produced by respiratory maneuvers. The circumstantial evidence in this case is rather strong.

*Syncope During Pressure Breathing and Breath Holding:* Support for the concept that changes in cardiac rhythm initiate a train of syncopal findings is found in the following case.

Case 5. C. A. N., a 38-year-old officer, was seen in consultation one year following a head injury. He has been asymptomatic. The patient was placed in the altitude chamber for a qualifying chamber flight. He was given 20 minutes of denitrogenation. He was monitored with an electroencephalogram, respirometer, and an electrocardiogram. At ground level the EEG was normal, his respirations were shallow and slow (12/min) and his heart rate was 84. There were no significant changes until pressure breathing altitude was reached. At 39,000 ft his heart rate was 108. At 42,000 ft the heart rate was 126 with deep respirations at 12/min. When the chamber leveled off at 43,000 ft, the rate of respiration was 12/min and deep, the heart rate was 120. Twenty-one seconds later (still at 43,000 ft) the heart rate began to slow and the patient experienced a sensation which he later described as reminding him of his feeling during hyperventilation. By 30 sec at 43,000 ft his pulse rate had slowed to 72/min. At that time the respirogram recorded a deep breath which was held for 16 sec. The patient later explained that he had held his breath voluntarily in order to combat hyperventilation. In the seventh second of breath holding, the heart rate slowed further to a rate of 46/min. It held to this rate even after breathing was resumed.

Twenty-three seconds after beginning breath holding his EEG showed evidence of marked generalized slowing, 4–6/sec activity (Fig. 8 and 9). After one minute at 43,000 ft and 25 sec after beginning of breath holding, the patient developed his first atrial premature systole. At 41 sec after the one deep inspiration the atrial premature systoles had recurred twice and the order to lower the chamber was given. Descent started 10 sec later. Atrial premature systoles appeared as intermit-

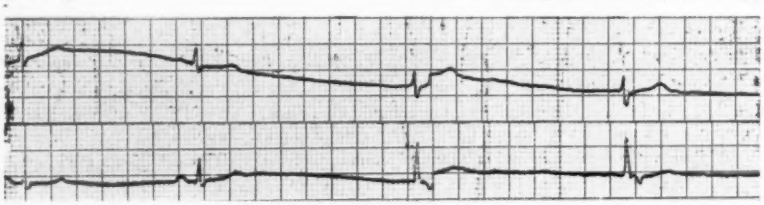


Fig. 7. Case 4. Two simultaneous leads demonstrating an example of slow lower nodal rhythm induced by holding the breath in deep inspiration. The subject developed syncope with this cardiac slowing.

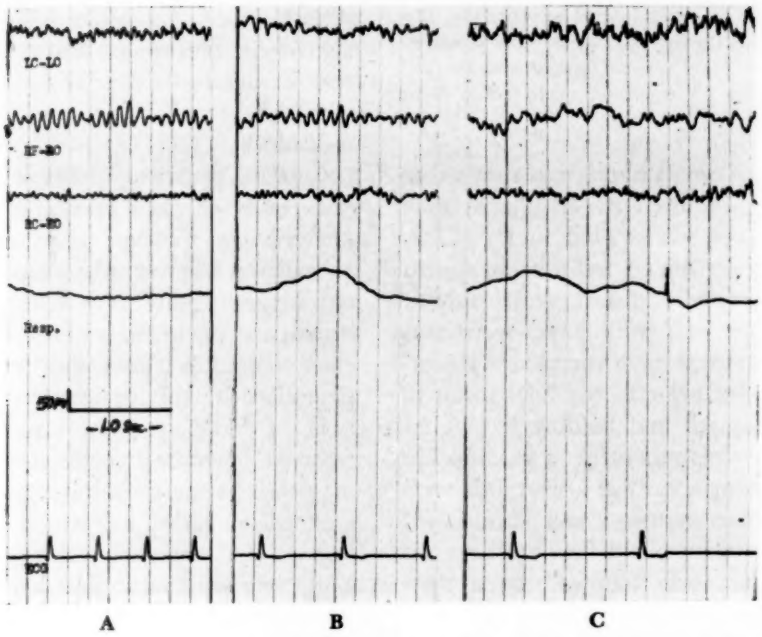



Fig. 8. Case 5. (A) Normal resting record at 42,000 ft (10/sec alpha activity). Heart rate 128. (B) 24–25 sec at 43,000 ft. There is some flattening of the EEG record (an attention pattern). Heart rate 75. (C) 55 sec of pressure breathing at 43,000 ft. Slow activity appears diffusely (4–6/sec activity). Heart rate 48.

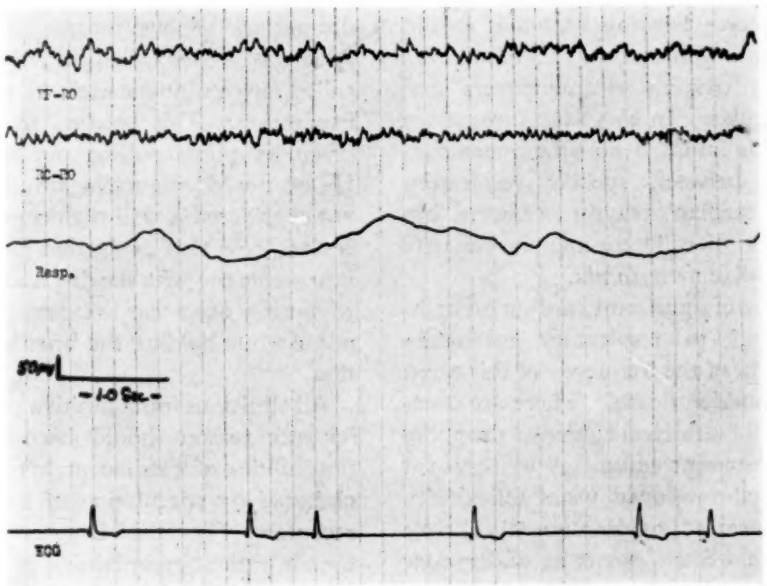



Fig. 9. Same patient as in Figure 8. 58–64 sec of pressure breathing. 28–34 sec. after deep inspiration. Diffuse slow activity continues (4–6/sec activity appears in bursts). Heart rate 42, with premature atrial beats.

tent coupling on the ECG and continued for 33 sec following this. The patient was conscious all this time. He was able to communicate immediately upon leaving the pressure breathing area. He commented, "I started to feel light." It was during the descent from pressure breathing altitude that the chamber crew first noticed clinical evidence that the patient was in difficulty. He had turned an ashen color and had begun to sweat. The rest of the flight was uneventful. His cardiac rate remained at 42/min. His respiratory rate had speeded up to 18/min. The slowed cardiac rate was present for at least 15 min after he had reached ground level.

Medical evaluation at ground level revealed no abnormalities. He was then cleared for another chamber flight. The second flight was performed and the patient was coached on his respiratory rate. The flight was uneventful.

The sequence of events in this case shows that the cardiac rate diminished a significant time before any changes were noted in the EEG. The EEG changes reflect central nervous system hypoxia secondary to diminished cardiac output. Pressure breathing may well have overstimulated the stretch receptors of the pleura initiating cardiac slowing prior to the final insult of taking a deep breath and holding it. A familiar chain of events was seen: a variation in respiratory mechanics, cardiac arrhythmia with diminished cardiac output, and diminished central nervous system blood flow with central nervous system hypoxia followed by a near syncopal episode.

## Discussion

Previous descriptions of the effect of the respiratory reflex on cardiac rate have stressed its marked variability. For this reason it should not be surprising to find marked variation in the relation between respiratory maneuvers and cardiac arrhythmias. In some instances, once the arrhythmia is initiated no subsequent consistent pattern between specific respiratory maneuvers and cardiac arrhythmia occurs, but rather a number of different maneuvers may precipitate a cardiac arrhythmia.

The occurrence of significant cardiac arrhythmias in relation to respiratory mechanics raises the question of the frequency of this event in unexplained sudden death. There are occasional accounts of athletes suddenly dropping dead from no apparent cause. A well-trained athlete has a well-developed vagal reflex with resting cardiac rates not infrequently below forty per minute. Such events as underwater swimming could easily create a hazard in susceptible individuals.

Changes in A-V conduction, intraventricular conduction and rhythms have now been noted with sufficient frequency to suggest that respiratory maneuvers of the type described in this report may be of help in evaluating many clinical problems, e.g., WPW syndrome, right bundle branch block, left bundle branch block, and ventricular bigeminy. Caution with such maneuvers should be exercised in those individuals with slow ventricular rates, e.g., in complete A-V block.

Certain practical applications have been made of the effects of respiration in creating such arrhythmias through experience. A simple Valsalva maneuver can cause fainting. The old squeeze game of children taking a deep breath and having someone squeeze the inflated chest commonly causes syncope. The usual explanation for this occurrence is decreased return of blood to the heart for mechanical reasons; however, the effects on cardiac rhythm may well be the most important aspect of such syncopal episodes. Early in aviation it was learned that the undesirable effects of G forces could be alleviated in part by tightening of the stomach muscles and taking a deep breath, thus enhancing venous return to the heart. If a true Valsalva maneuver of bearing down against a closed glottis was done syncope was apt to follow. Such syncopal episodes were ascribed to diminished venous return. A modified Valsalva was devised called the M1 maneuver which called for continuous expiration after maximum inspiration. This became the yell commonly given by pilots pulling out against G forces. Unless the M1 maneuver was a noisy one it was not considered a well performed maneuver. It is clear now that expiration has another effect: it prevents the peak slowing and the possibility of triggering off a cardiac arrhythmia that may occur while holding the breath in deep inspiration.

All clinicians using positive pressure breathing for any reason should become aware of the possibilities of cardiac arrhythmias being precipitated by stimulation of the pleural stretch receptors. The clinician should also be aware that a patient complaining of cardiac arrhythmia may be unconsciously inducing arrhythmias by hyperventilation or other respiratory maneuvers.

In the past it has been customary to advise individuals who hyperventilate to hold their breath when they note hyperventilation. In the light of observations in the cases reported here, this seems to be rather poor advice in cer-

tain instances. Perhaps it would be better to advise hyperventilators merely to count their respiration, consciously regulating the rate to a fixed number (perhaps 10) per minute while keeping their breathing shallow. Certainly in the case of a susceptible individual in primary control of aircraft a deep breath to control hyperventilation (followed by cardiac arrhythmia and syncope) may well be the last breath he ever takes.

## Summary

Significant cardiac arrhythmias have been induced by simple respiratory maneuvers, breath holding and hyperventilation. Marked cardiac slowing, passive nodal rhythm and cardiac arrest have been noted. Arrhythmias are apparently initiated by stimulation of pulmonary stretch receptors. Syncope may be precipitated. The case of an aircraft accident involving a pilot with one of these mechanisms is discussed. Examples of various arrhythmias is included. The possible role of this mechanism in sudden unexplained death is pointed up.

## Addendum

Since conclusion of this paper we have observed cardiac arrest of over 12 seconds with breath holding. Large doses of atropine have successfully prevented cardiac arrest and prevented syncope on repeated trials.

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# The Cube Vectorcardiogram in Various Degrees of Right Bundle Branch Block*

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IT HAS been alleged by some authors[1] that the horizontal QRS loop of the cube vectorcardiogram may be employed to distinguish right ventricular hypertrophy from right bundle branch block. Clockwise inscription of this loop is regarded as typical of right ventricular hypertrophy and the slow inscription of the final limb of the loop is regarded as typical of delayed conduction in the right bundle branch (Fig. 1). Although clockwise inscription of the horizontal QRS loop in "atypical" right bundle branch block has been recorded by these authors no evidence is furnished that clockwise inscription of the loop may not also occur as a result of lesser degrees of right bundle branch block, and no evidence is furnished that the slow inscription of the final limb of the loop is necessarily present in these same lesser degrees of right bundle branch block. As a matter of fact the important hiatus that is found upon close examination of the basis of these allegations is the lack of any recorded observations of the effect of various degrees of right bundle branch block upon the vectorcardiogram when no right ventricular hypertrophy is present.

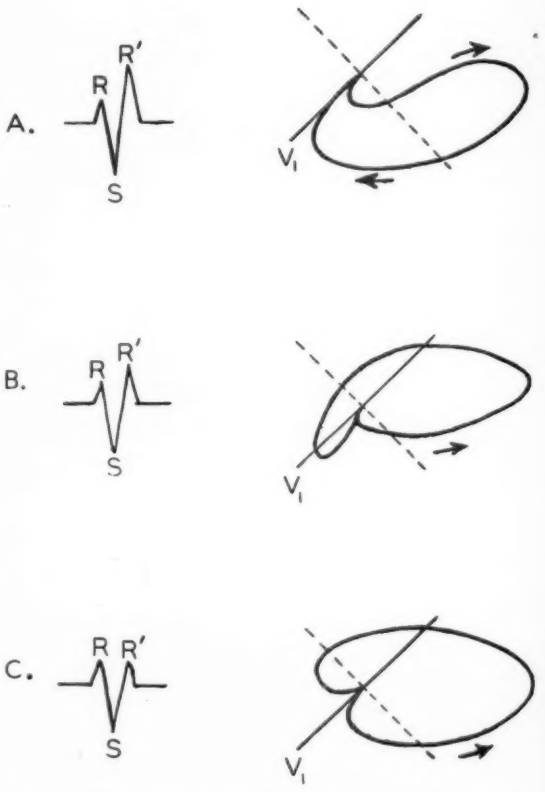


Fig. 1. Diagrams of the horizontal loop of the cube vectorcardiogram allegedly characteristic for (A) right ventricular hypertrophy, (B) right bundle branch block, (C) normal, when precordial lead $V_1$ shows an RSR′ pattern. (Reproduced from Grishman, A.: *Pediatrics* 17: 100, 1956.)

The opportunity to make such observations is rare. However, recently one of us (I. L. R.) encountered a patient whose electrocardiogram showed varying degrees of delay of conduction in the right bundle branch (Fig. 2 and 3). In this case normal conduction could be observed after slowing by carotid sinus stimulation (see Fig. 2B and 3); intermediate degrees of block were common, and a higher degree of block could be observed when the rate was increased by a short period of hyperventilation (Fig. 2A). Electrocardiograms and corresponding vector-

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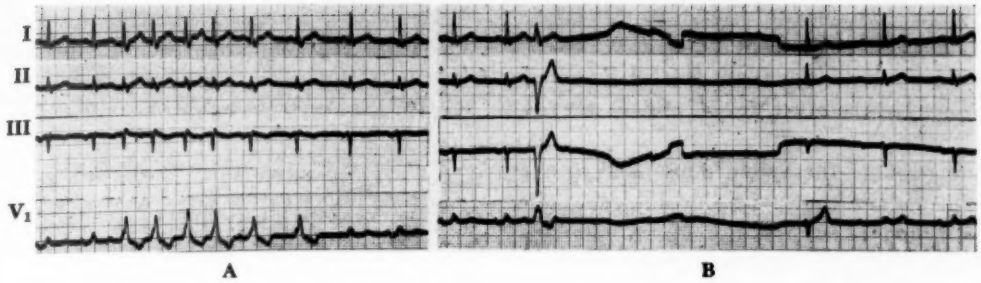


Fig. 2. Electrocardiograms recorded while deliberately inducing varying degrees of disturbance in conduction in the right bundle branch in our subject. (A) Leads I, II, III, and $V_1$ simultaneously recorded during a short period of rapid breathing. Note increase in degree of block with shorter cycle lengths (incidentally, the P-R interval is longer during the shorter cycle lengths). (B) Leads I, II, III, and $V_1$ simultaneously recorded during slowing of the rate by carotid sinus pressure. Note that the beat following the long pause shows no recognizable degree of bundle branch block. The succeeding beats show progressively increasing degree of block.

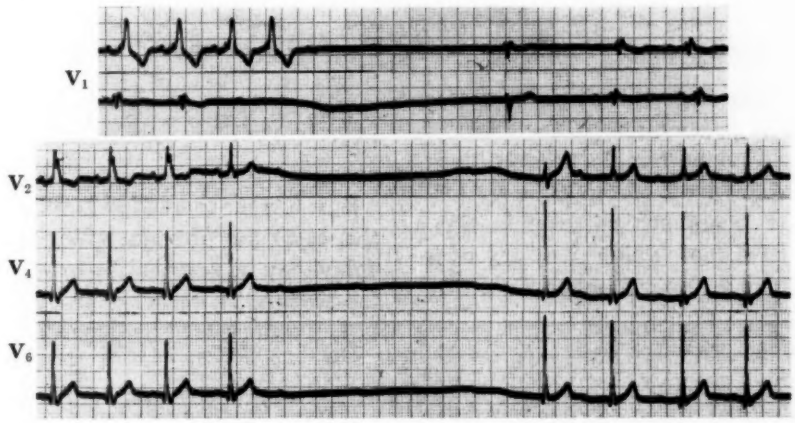


Fig. 3. Lead $V_1$ showing varying degrees of right bundle branch block which is abolished in the beat following the long pause induced by carotid sinus stimulation. The cycle after the long pause shows normal conduction. Leads $V_2$, $V_4$, and $V_6$ recorded simultaneously show the same phenomena.

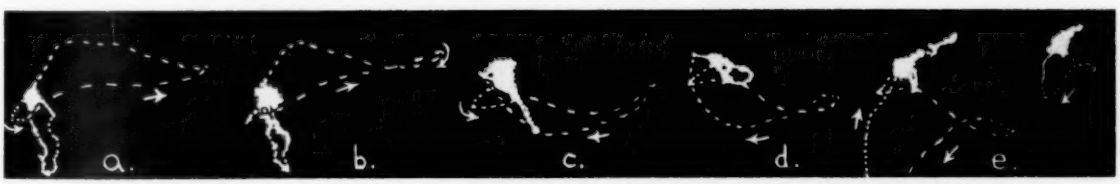


Fig. 4. Horizontal loops of the cube vectorcardiogram recorded while varying the degree of right bundle branch block in the same subject by changing the rate. The changes in rate were induced by hyperventilation and by carotid sinus stimulation. (*a*) Presumably normal conduction. (*b*) Possibly a respiratory variant of (*a*) or (*c*). (*c*), (*d*), (*e*) Increasing degrees of right bundle branch block, respectively.

cardiograms were recorded in the presence of several degrees of right bundle branch block (Fig. 4). All of the records shown were obtained within a period of less than one hour.

The subject from whom these records were made is a 74-year-old man who on fluoroscopy exhibits no evidence of hypertrophy or of enlargement of the right ventricle. Regardless of the presence or absence of such evidence it must be apparent that the variations seen in the loops and in the electrocardiograms must be largely due to changes in conduction in the right bundle branch. Right ventricular hypertrophy could not appear and disappear within a few minutes'

time. Right ventricular dilatation should be more marked after the long pause induced by carotid sinus stimulation; yet it is at this time that the normal records (Fig. 2B and 3) are obtained.

Examination of the QRS loops of Figure 4 makes it evident that with incomplete right bundle branch block the horizontal loop recorded with the cube method may develop precisely the same characteristics that are allegedly typical of right ventricular hypertrophy; they are inscribed clockwise and anteriorly (compare with Figure 1A). It is also to be noted that the terminal portion of the QRS loop is inscribed slowly only in the presence of a high degree of block (Fig. 3).

## Discussion

The records made from this single rare case constitute the only presentation of the effect of various degrees of right bundle branch block upon the horizontal loop of the cube vectorcardiogram that bears critical examination. Certainly they have more value than any conclusions drawn from a larger number of cases by inference alone.

The observations presented in Figure 4 show that clockwise and anterior inscription of the horizontal QRS loop recorded by the cube method may occur solely as the result of various degrees of right bundle branch block. Since precisely the same finding can be observed in the presence of right ventricular hypertrophy, it follows that this finding (clockwise inscription of the horizontal vectorcardiogram, Figure 1A), when encountered, is of no value in distinguishing right ventricular hypertrophy from right bundle branch block. Either or both conditions may be present.

It should be stated that we do not believe that in right bundle branch block the horizontal loop of the cube is invariably inscribed as shown in Figure 4. It is frequently inscribed in a counterclockwise manner. This subject will be dealt with in greater detail in another paper.

## Summary and Conclusions

Observations of the effect of varying degrees of right bundle branch block in the same individual prove that the QRS loop of the horizontal vectorcardiogram recorded by the cube method may be inscribed in a clockwise manner solely as a result of this conduction disturbance and that the terminal portion is inscribed slowly only in more advanced degrees of block.

It is concluded that clockwise inscription of the QRS horizontal loop as diagrammed in Figure 1A, when encountered, may not be employed to distinguish right ventricular hypertrophy from incomplete right bundle branch block. Either or both conditions may be present.

It is further concluded that occasionally (as in this case) the presence of right bundle branch delay may be revealed by its modification when the heart rate is decreased by carotid sinus stimulation, or increased by hyperventilation.

## Addendum

Since the completion of this paper Sodi-Pallares and co-workers have published (Am. J. Cardiol. 1: 57, 1958) the results of investigations of the same problem. They also conclude that the loop in incomplete right bundle branch block may be inscribed in a clockwise manner. It is also evident in their data that the terminal limb of the loop is not inscribed slowly in incomplete right bundle branch block.

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# Atypical Wenckebach Periods with Dropped Atrial Beats*

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SECOND DEGREE A-V block, type I, is characterized by groups of sinus beats which are conducted to the ventricle with increasing delay. They are separated by pauses which are caused by failure of the A-V bundle to transmit a sinus impulse to the ventricle. The increment in A-V conduction time within each group is typically greatest in the second beat after the pause.[1] This type of A-V block is usually referred to as Wenckebach periods.

The case to be reported here presented Wenckebach periods which were atypical in two respects. First, the longest increment in A-V conduction time occurred in the last beat of the group. Second, intermissions often were caused by dropped atrial rather than ventricular beats. Atrial intermissions were tied to a certain length of A-V conduction time in the preceding beat.

## ELECTROCARDIOGRAPHIC FINDINGS

A. B., a 59-year-old man, was treated for the first time in the Maimonides Hospital in 1955 for hypertensive encephalopathy. He had diabetes and angina pectoris on effort. Following digitalization a P-R interval of 0.40 sec was observed; 11 days later it had decreased to 0.25 sec.

The patient was admitted for a second time on October 29, 1957 when he suffered a posterior wall myocardial infarction. The A-V conduction time was then normal. After digitalization second degree A-V block developed.

Figure 1 shows a fairly regular sinus rhythm; the length of the atrial cycle ranges from 0.92 to 0.98 sec. There are two groups of 4:3 Wenckebach periods separated by a period of 2:1 A-V block ($P_5$-$P_6$). In the group $P_1$-$P_4$ the P-R interval increases from 0.22 to 0.29, and then to 0.42 sec; $P_4$ is blocked. In the group $P_7$-$P_{10}$ the P-R interval increases from 0.21 to 0.28 and 0.38 sec; $P_{10}$ is blocked. In both groups the increment of the P-R interval is greater in the third than in the second beat.

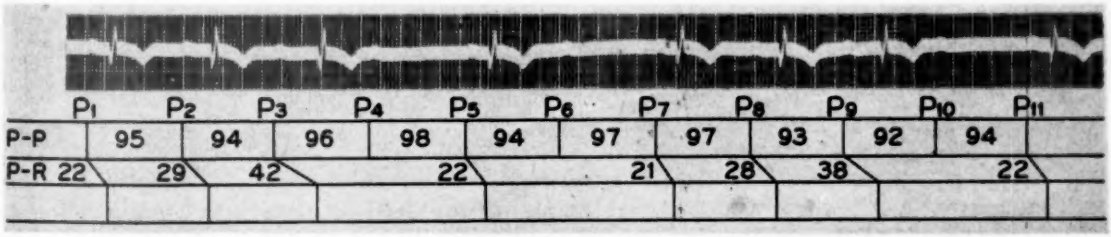


Fig. 1. Lead aVF. $P_1$-$P_4$ and $P_7$-$P_{10}$ represent genuine Wenckebach periods. They show a progressive increase of the P-R interval, but the increment is greatest in the last beat of each group. The pauses following each group are due to blocked atrial excitations ($P_4$ and $P_{10}$); $P_5$-$P_6$ represent 2:1 A-V block. (Time intervals are expressed in $^1/_{100}$ sec.)

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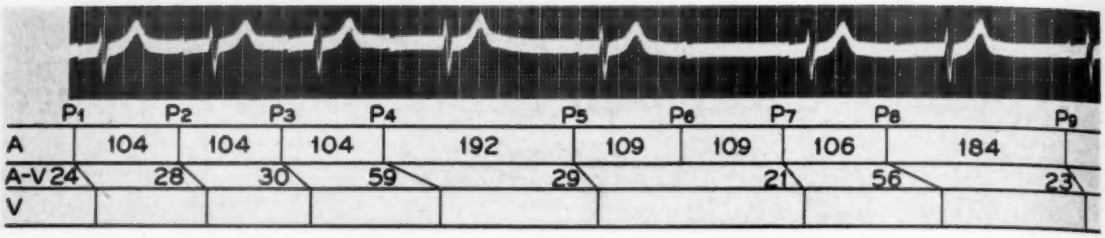


Fig. 2. Lead $V_1$. The first 4 beats ($P_1$-$P_4$) resemble a Wenckebach period, in that the P-R interval increases from 0.24 to 0.59 sec. The greatest increment in A-V conduction time is shown by the last beat of the group ($P_4$). The long pause following $P_4$ measures 1.92 sec, that is, less than two sinus cycles. It contains no P wave. Therefore, the pause is due to an atrial intermission. $P_5$-$P_6$ represent a 2:1 A-V block. Then a group of two conducted beats follows ($P_7$-$P_8$), in which the P-R interval increases from 0.21 to 0.56 sec. An atrial intermission between $P_8$ and $P_9$ causes a pause which, again, is shorter than two sinus cycles.

Figure 2 shows a basically regular sinus rhythm whose atrial cycle length varies from 1.04 to 1.09 sec. The group $P_1$-$P_4$ seems to represent a Wenckebach period. In successive beats the P-R interval increases from 0.24 to 0.28, 0.30, and then abruptly to 0.59 sec. There follows an intermission in which no P wave is discernible. The pause $P_4$-$P_5$ measures 1.92 sec, that is, less than two sinus cycles. The group $P_5$-$P_6$ shows 2:1 A-V block. In the last group $P_7$-$P_8$, the P-R interval increases from 0.21 to 0.56 sec. Then a pause follows which is due to an atrial intermission; it lasts 1.84 sec, again less than two sinus cycles, and is followed by $P_9$.

Figure 3 shows two tracings which were taken before and after injection of atropine. Tracing A presents a basically regular sinus rhythm with a cycle length of 0.94–0.98 sec. A 2:1 A-V block predominates. Only in the group $P_3$-$P_4$ two successive sinus beats are conducted to the ventricle, the P-R interval increasing from 0.22 to 0.51 sec. Then a long pause follows in which no P wave is discernible; it measures 1.73 sec, while the double sinus period is 1.92 sec.

Tracing 3B was taken 40 minutes after intramuscular injection of 1/75 gr of atropine. There is regular sinus rhythm, the cycle length measuring 1.01 sec. Each sinus excitation is now conducted to the ventricle after a P-R interval of 0.28 sec. Through the effect of atropine the second degree A-V block has been converted to first degree block, with no significant change in the duration of the sinus period.

## Discussion

This case presents unusual deviations from the typical pattern of Wenckebach periods. The increment in A-V conduction time is longest in the last instead of the second beat of each group. Some groups represent a true Wenckebach phenomenon with dropped ventricular beats (Fig. 1). Most of the intermissions, however,

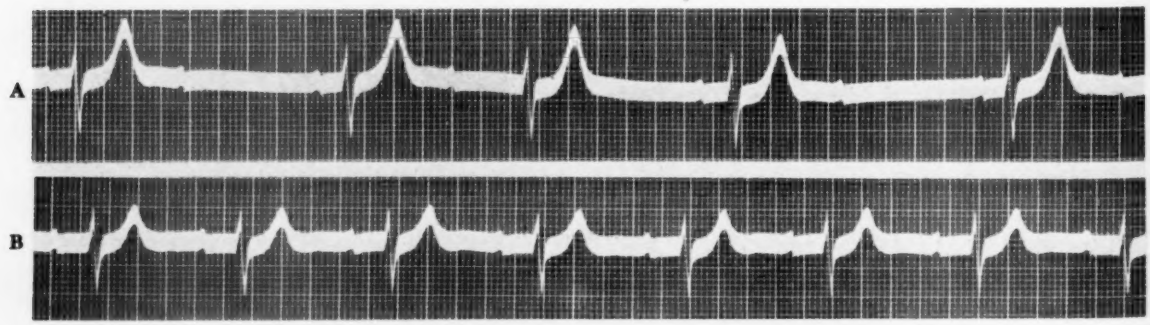


Fig. 3. Lead $V_1$. Tracing A shows a predominant 2:1 A-V block. Only $P_3$ and $P_4$ are conducted in succession, the P-R interval increasing from 0.22 to 0.51 sec. The pause following $P_4$ is due to an atrial intermission. Tracing B was taken after injection of atropine. There is now a first degree A-V block. The P-R interval measures 0.28 sec.

are caused by dropped atrial beats. The pauses are invariably shorter than two sinus cycles. Were a regular P wave hidden in a ventricular complex, the long atrial interval would obviously equal two sinus periods. Diligent search revealed neither regular nor premature P waves during the long pauses in numerous tracings in which this phenomenon was observed. Atrial intermissions were closely related to the length of the A-V conduction time of the beat preceding the intermission. It occurred regularly whenever the P-R interval abruptly increased to 0.50 sec or more, the increment in A-V conduction time often equaling or exceeding the P-R interval of the preceding beat.

Dropped atrial beats in the presence of first degree A-V block can be readily mistaken for true Wenckebach periods. In the text of Wenckebach and Winterberg[1] a case is described (Fig. 236 and 238) which closely resembles the one here reported. In their Figure 238, the P-R interval advances in seven successive beats from 0.17 to 0.26 sec. In the 8th beat, there is an abrupt increase of the A-V conduction time to 0.42 sec. Then a long pause follows which the authors erroneously attribute to a dropped ventricular beat. Actually no P wave is discernible during the pauses between conducted sinus excitations.

The mechanism of the dropped atrial beats must be considered in connection with the other abnormality to which it is invariably tied, namely, the abrupt marked increase of the P-R interval in the beat preceding the intermission. Wenckebach and Winterberg express the view that the atypical increase of the A-V conduction time in the last beat of a group is not determined by the properties of the conduction disorder but by extrinsic influences such as vagus effect. It is plausible that sudden rise in the vagus tone may cause further impairment of A-V conduction and, in disposed individuals, inhibition of impulse formation in the sinus pacemaker. A case of Wenckebach periods was reported[2] in which the conduction disturbance was related to the respiratory cycles, apparently caused by periodic increase of the vagus tone. In our own case, injection of atropine converted the second degree into first degree A-V block and caused disappearance of the atrial intermissions.

Wallace and Katz[3] and Katz and Pick[4] observed instances of first and second degree A-V block with atrial intermissions which, unlike our own case, were not related to undue prolongation of the P-R interval of the beat preceding the intermission. These authors thought that the long atrial intervals were caused by sinoatrial block. It was previously mentioned that in our case the atrial pauses were invariably shorter than two sinus cycles. This may occur when the sinoatrial block is of the type I, analogous to the Wenckebach periods of A-V block. If this is the case, the spacing of the atrial beats should be similar to that of the ventricular beats in Wenckebach periods; that is, in each group the first atrial cycle after the pause is expected, in typical instances, to be longer than the succeeding cycles. This relationship was not observed in our case; for instance, in Figure 2, the atrial cycles of the first group measure constantly 1.04 sec. It seems that in our case vagus stimulation caused, simultaneously with marked prolongation of the A-V conduction time, inhibition of the sinus pacemaker. The vagus effect may have been related to digitalization.

It is of interest that atrial intermissions were never observed following dropped ventricular beats. The latter phenomenon was apparently due to properties inherent in the A-V conduction defect rather than to vagus effect.

## Summary

A case of Wenckebach periods is reported which was atypical in two respects. (1) The greatest increment in A-V conduction time occurred in the last beat of the group. (2) The pauses between groups of conducted beats were due more often to atrial rather than ventricular intermissions. Atrial intermissions were invariably tied to an abrupt, marked increase of the A-V conduction time of the preceding beat.

Both phenomena, atrial intermissions and abrupt prolongation of the A-V conduction time immediately preceding the intermission, are explained by vagus effect. They were abolished by the action of atropine.

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# Report on Therapy

# The Treatment of Auricular Arrhythmias with Deslanoside*

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PAROXYSMAL auricular arrhythmias represent a source of acute discomfort to the patient and may, in older people, precipitate peripheral vascular collapse and congestive heart failure. The treatment of these arrhythmias presents a challenge to the physician and particularly to the resident staff of a general hospital where such cases constitute a frequent source of emergency room admissions.

In recent years, rapidly acting digitalis preparations have gained increasing use and acceptance as effective and safe treatments of these arrhythmias, with lanatoside C widely employed as a drug of choice.[1–3] This has been replaced recently by deslanoside† (desacetyl lanatoside C) for parenteral administration. They act rapidly when injected intravenously, showing initial effects within ten minutes, and are dissipated more quickly than most other products, thus lessening the duration of action and toxicity. Deslanoside (hereafter referred to as cedilanid-D) is formed by subjecting lanatoside C to mild alkaline hydrolysis, resulting in a chemically stable product with a gravimetrically standardized dosage. Being more soluble than the parent glycoside, cedilanid-D is suitable for both intravenous and intramuscular administration.

Hoesley and Luan[4] have described cedilanid-D as the drug of choice for rapid digitalization. They point out that speedy digitalization is imperative in cases of auricular fibrillation with a rapid ventricular rate and acute congestive heart failure following myocardial infarction. They suggest an initial intravenous injection of 0.8 mg followed by 0.2 mg every two to four hours depending upon clinical considerations. Winsor and Khoury[5] administer 1.6 mg of cedilanid-D intramuscularly as an initial dose in auricular flutter, followed by 0.4 mg two hours later. They also find it effective in the treatment of paroxysmal auricular tachycardia, especially if pressure is applied to the carotid sinus 20 to 30 minutes after the injection.

Sanazaro[6] has recently reported on his extensive study of cedilanid-D, in which various facets of its application were explored. His results in the treatment of the supraventricular arrhythmias indicated that cedilanid-D retains the pharmacologic characteristics of lanatoside C. He noted that therapeutic effects began within minutes and were usually complete in one or two hours, and that toxicity was uncommon, minor, and short-lived.

These observations provide evidence of the similarity of cedilanid-D to lanatoside C. The effectiveness of the latter agent in the treatment of paroxysmal auricular tachycardia has been documented in numerous publications. Weisberger and Feil[7] reported extremely favorable results in 16 patients, while Barrow[8] obtained similar results in 26 patients. He cited the absence of toxicity as contributing to its clinical usefulness, an estimate supported by the observations of Morris[9] and Weisberg.[10]

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† U.S.P.XV. Available as cedilanid-D in ampuls of 2 cc (0.4 mg) and 4 cc (0.8 mg), manufactured by Sandoz Pharmaceuticals.

The purpose of the present paper is to present our results with cedilanid-D in the treatment of various paroxysmal auricular arrhythmias.

## Method of Study

The study was divided into two parts: (1) An effort was made to determine the efficacy, rapidity of action, and toxicity of cedilanid-D in a small group of patients with chronic auricular fibrillation. (2) The drug was administered to patients with paroxysmal auricular arrhythmias to determine its effectiveness in the conversion of these aberrant rhythms.

First, an attempt was made to ascertain whether the patient had received digitalis prior to his hospital admission, since this guided us in the selection of dosage. If no digitalis had been taken, an initial dose of 0.8 mg cedilanid-D was injected intravenously, followed by 0.4 mg in two hours, and 0.4 mg two hours later. The drug was administered intramuscularly in a few patients, where intravenous injection was not possible. If the patient had been on digitalis maintenance or had received some digitalis before arrival, the initial injection was 0.4 mg intravenously, followed by 0.4 mg intravenously at two- to four-hour intervals until the desired clinical effect was achieved or the total dose of 1.6 mg was reached. In no case was a total dose of 1.6 mg exceeded. In those patients known to have received digitalis prior to admission, care was taken to obtain an electrocardiogram in an effort to determine the degree of digitalization.

## Case Histories

### CHRONIC AURICULAR FIBRILLATION

Group I consists of four patients with rapid auricular fibrillation and congestive heart failure.

Case 1. A. M., a 76-year-old white female, was admitted on October 20, 1957 with a chief complaint of sudden onset of dyspnea and palpitation of one day's duration. There was no past history of cardiovascular disease or use of digitalis. On physical examination, the blood pressure was 140/100, respirations were 35 and the apical heart rate was 200, with a grossly irregular rhythm. There were fine crepitant rales throughout both lung fields and 4+ pretibial edema.

Ten minutes after 0.8 mg cedilanid-D was injected intravenously, the apical rate fell to 120. An electrocardiogram taken at this time showed auricular fibrillation. One hour and forty-five minutes later, the apical rate fell to 100. Relief of dyspnea paralleled the reduction in the apical rate. The patient was maintained on digoxin and mercurial diuretics and was discharged one week later, well compensated.

Case 2. A. G., a 73-year-old white female, was admitted on October 7, 1957 with a history of fever, chills, dyspnea, and anorexia of 24 hours' duration. She was a known diabetic and had been careless with her insulin dosage. On the morning of admission, she had become semicomatose. To our knowledge, she had never received digitalis.

Examination revealed a blood pressure of 190/80, rectal temperature of 104° F, and respirations of 40/min. The apical rate was 128/min and irregular. The patient was semicomatose. There were coarse, moist rales in both lung fields, and marked ankle and pretibial edema. She showed 4+ glucose and 2+ acetone in the urine. Admission blood sugar was 400 mg. An electrocardiogram revealed auricular fibrillation and changes of myocardial ischemia.

The patient received 1.6 mg cedilanid-D in divided doses intravenously over an 8-hour period with slowing of the apical rate to 85/min. The patient made a good response to small doses of insulin, dehydration, and antibiotics, and was then placed on a maintenance regimen of oral digitoxin. Two weeks later she was discharged with a diagnosis of diabetic coma, arteriosclerotic heart disease, and chronic auricular fibrillation.

Case 3. P. A., a 67-year-old white male, was seen in a physician's office five days prior to admission. He complained of dyspnea, orthopnea, and edema of the legs. Physical examination at that time revealed an apical rate of 120/min. He was digitalized with 1.2 mg of digitoxin orally over a period of 48 hours.

On the day of admission to the hospital, there had been little change in his condition and the apical rate remained at 120. The patient was redigitalized with cedilanid-D, receiving 0.8 mg intravenously on admission and another 0.8 mg intravenously four hours later. At the end of seven hours, the apical heart rate had fallen to 74 although he continued to fibrillate. Recovery was uneventful and the patient was discharged 12 days later.

CASE 4. A. A., a 67-year-old white male, was admitted to the emergency ward in a semicomatose condition on June 29, 1957. Physical examination revealed a blood pressure of 100/70, respirations of 35 per minute, and rectal temperature of 101° F. Positive physical findings were marked dehydration, cyanosis, and a grossly irregular apical heart rate of 140–180. The electrocardiogram, taken on admission, revealed auricular fibrillation with a ventricular rate of 160–200.

Cedilanid-D, 0.8 mg, was given intravenously on admission, 0.4 mg intravenously in two hours, and another 0.4 mg two hours later. Two hours after the initial dose the apical rate fell to 88 with persistence of the auricular fibrillation. The patient apparently was making a normal recovery when he developed a severe hypostatic pneumonia and died on July 5, 1957.

*Comment:* The results of treatment in this group of four patients show that cedilanid-D is effective in lowering the ventricular rate rapidly. This is graphically shown in Figure 1. The low incidence of toxicity is very well illustrated in case 3 where the patient had been previously digitalized and yet responded dramatically to intravenous administration of cedilanid-D. These patients were all chronic fibrillators and no attempt was made to convert them to normal sinus rhythm.

## PAROXYSMAL AURICULAR ARRHYTHMIAS

Group II consists of nine cases of paroxysmal auricular arrhythmias which were treated with cedilanid-D and converted to normal sinus rhythm.

CASE 5. P. S., a 75-year-old Negro woman, was admitted to the hospital on October 25, 1957. She had been complaining of upper respiratory distress for two days prior to admission. About 24 hours before admission, she began to develop severe dyspnea and orthopnea. There was no history of heart disease and to her knowledge she had never received digitalis.

Physical examination showed an acutely dyspneic and orthopneic patient. The blood pressure was 160/100 and respirations were 35/min. The apical rate was 140 and the rhythm irregular. The patient was wheezing and there were bilateral, fine generalized crepitant rales. The clinical diagnosis was auricular fibrillation with congestive heart failure.

On admission she received 0.8 mg cedilanid-D intravenously, 0.4 mg in four hours and 0.4 mg four hours later. The electrocardiogram eight hours after admission showed normal sinus rhythm at a rate of 98. The patient recovered uneventfully and was in normal sinus rhythm on discharge from the hospital two weeks later.

CASE 6. H. P., a 66-year-old white male, was admitted on February 11, 1957 with the chief complaints of dizziness, chills, sweating, emesis, and diarrhea occurring immediately after eating supper on the night of admission. The patient had been well prior to the onset

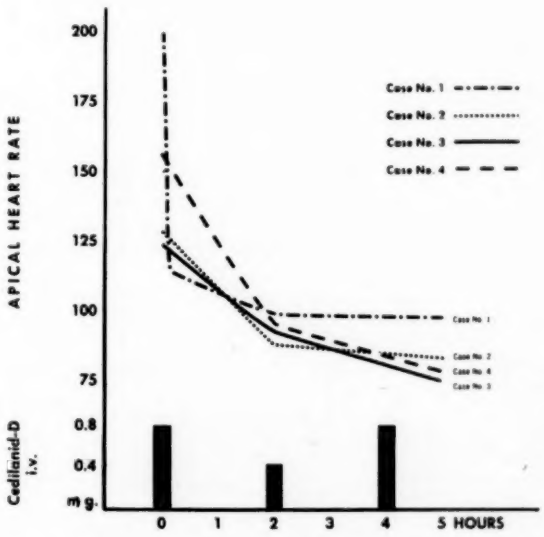


Fig. 1. Response of ventricular rate to intravenous injection of cedilanid-D in four cases of auricular fibrillation. Only case 4 received a second dose of 0.4 mg cedilanid-D.

of these symptoms and had never received digitalis. Physical examination revealed a blood pressure of 110/80 and a regular apical heart rate of 70/min. The remainder of the physical examination was negative.

An electrocardiogram taken on admission showed impure auricular fibrillation with a ventricular rate of 95–120 (Fig. 2A). At this time he was given cedilanid-D 0.8 mg intravenously. An electrocardiogram taken two hours later showed auricular fibrillation with runs of auricular flutter and 2 : 1 A-V block. At this time another injection of 0.8 mg cedilanid-D intravenously was made. Two hours later a repeat electrocardiogram showed normal sinus rhythm at a rate of 60/min. The gastroenteritis responded to routine treatment. Recovery was uneventful and the patient was discharged four days later in normal sinus rhythm.

Case 7. H. B., a 50-year-old white male, was admitted on September 19, 1957 to the surgical service for elective repair of a diaphragmatic hernia. Symptoms on admission included intermittent epigastric pain, moderate dyspnea, and one episode of syncope.

Physical examination revealed a blood pressure of 130/100, and an irregular apical heart rate of 120/min. The patient had a negative history for cardiovascular disease and had never been treated with digitalis. An electrocardiogram on admission showed auricular fibrillation with a ventricular response of 150–155. The next day the rhythm reverted to normal without any treatment.

Two weeks after admission the electrocardiogram revealed a return to auricular fibrillation which would not revert spontaneously (Fig. 2B). He was then given cedilanid-D 0.8 mg intravenously, 0.4 mg two hours later, and another 0.4 mg two hours after that. One-half hour after the latter dose, the rhythm returned to a normal sinus rhythm, confirmed by electrocardiogram. The patient underwent surgery uneventfully and was discharged one month after admission in normal sinus rhythm.

Case 8. A. K., a 66-year-old white female,

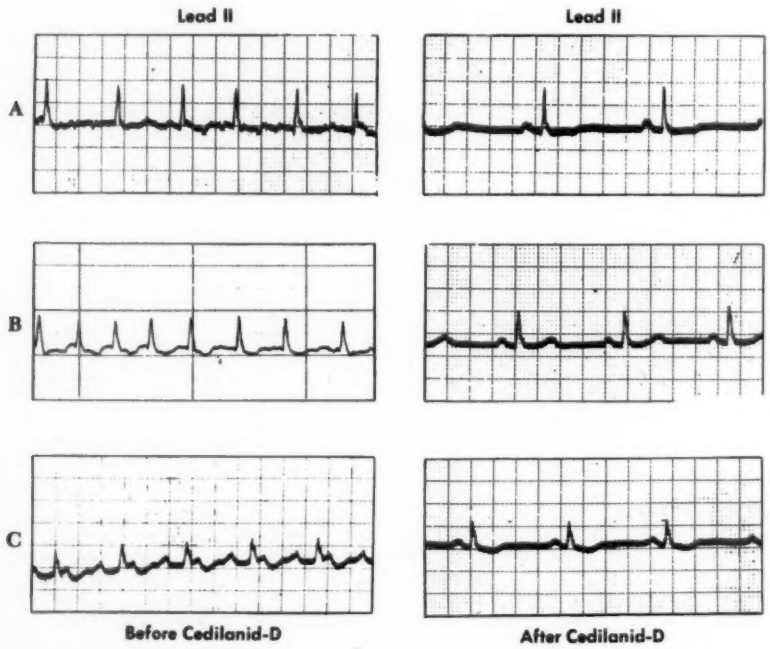


Fig. 2. (A) Case 6. Paroxysmal auricular flutter-fibrillation, reverting to normal after two injections of 0.8 mg cedilanid-D. (B) Case 7. Paroxysmal auricular fibrillation reverting to normal after 1.6 mg cedilanid-D intravenously. (C) Case 8. Auricular flutter with 2:1 A-V block, reverting to normal sinus rhythm after 1.2 mg cedilanid-D intravenously.

was admitted on August 29, 1957. The patient had had rheumatic heart disease for many years. Over a three-year period she had been experiencing episodes of rapid heart action. One and one-half years prior to this admission she had developed dyspnea and ankle edema and complained of heart palpitations.

Physical examination revealed a grade II diastolic murmur at the apex and an apical heart rate of 108. The admission electrocardiogram showed auricular flutter with 2 : 1 block (Fig. 2C). She was given cedilanid-D 0.8 mg intravenously and 0.4 mg intravenously three hours later. A repeat electrocardiogram the next morning revealed normal sinus rhythm. The patient was discharged two days after admission on maintenance digitalis and in normal sinus rhythm.

CASE 9. S. C., a 36-year-old white male, was admitted on April 14, 1957 complaining of a "fluttering" precordial sensation which came on suddenly while at work. One year prior to admission the patient had experienced a rather severe attack of rapid heart action which was diagnosed by a physician as paroxysmal auricular tachycardia. The attack was terminated by carotid sinus pressure.

On admission, the electrocardiogram revealed paroxysmal auricular tachycardia with a rate of 200. The tachycardia was not affected by carotid sinus pressure or routine methods of vagal stimulation. Forty-five minutes after an intravenous injection of 0.8 mg cedilanid-D, the arrhythmia converted to normal sinus rhythm. He was discharged the next morning without any further treatment.

CASE 10. S. M., a 66-year-old white female, was admitted on September 24, 1957. The patient underwent a left upper lobectomy for carcinoma and had an uneventful postoperative recovery for ten days. During the next five days the patient showed increasing orthopnea, ankle edema, jugular venous distention, and developed bilateral pulmonary rhonchi. She

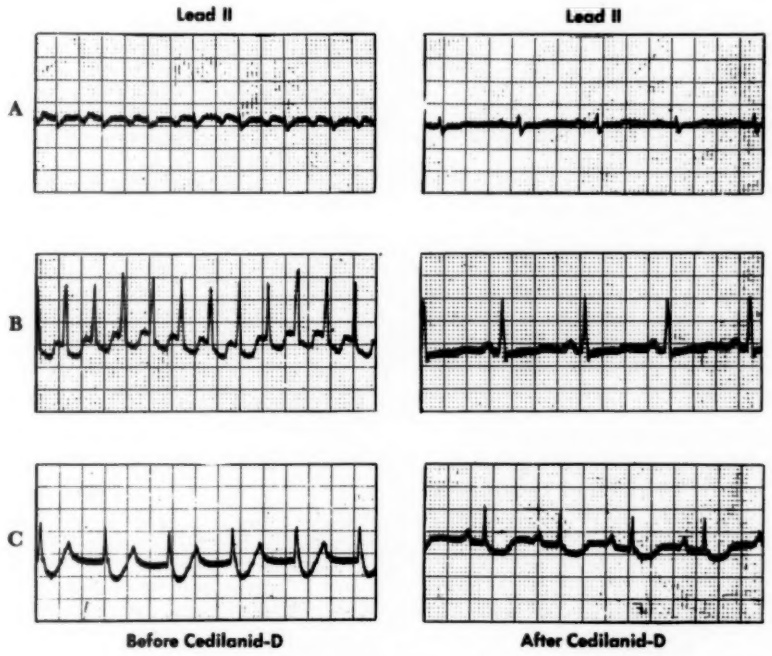


Fig. 3. (A) Case 10. Paroxysmal 2:1 auricular flutter, reverting to normal sinus rhythm after two 0.4 mg doses of cedilanid-D intravenously. (B) Case 11. Paroxysmal auricular tachycardia, reverting to normal sinus rhythm after 1.6 mg cedilanid-D intravenously in divided doses. (C) Case 13. Nodal tachycardia, reverting to normal sinus rhythm after 1.2 mg cedilanid-D intravenously in divided doses.

was digitalized slowly with considerable relief of symptoms, and was then placed on maintenance digitalis.

On the 15th postoperative day, the apical pulse rose to 150/min and the electrocardiogram showed auricular flutter with 2 : 1 heart block (Fig. 3A). The patient was given 0.4 mg of cedilanid-D immediately and 0.4 mg two hours later. An electrocardiogram taken after the last dose showed a return to normal sinus rhythm. Recovery was uneventful and the patient was discharged four weeks after admission in normal sinus rhythm and on digitalis maintenance.

Case 11. M. C., a 23-year-old white female, was admitted to St. Vincent's Hospital in May 1957 because of rapid heart action. She had had several similar episodes varying in duration from two hours to three days, precipitated by overactivity. The present episode had started about one hour prior to admission.

Physical examination revealed a rapid regular apical rate of 200 and a blood pressure of 90/70. There were no other abnormal cardiac findings. The lung fields were clear. An electrocardiogram revealed paroxysmal auricular tachycardia (Fig. 3B).

This patient had been on maintenance digitalis and quinidine but the intake of both medications had been extremely irregular. She was given 0.8 mg of cedilanid-D intravenously followed in four hours by another dose of 0.8 mg. Within three hours, the tachycardia reverted to normal sinus rhythm.

Case 12. H. B., a 67-year-old male, was admitted to St. Vincent's Hospital in December 1957 because of a tumor of the descending colon. Five years prior to admission he had suffered a small posterior wall myocardial infarction. An electrocardiogram on admission had shown complete disappearance of the post-infarction changes. On December 9 a resection of the sigmoid colon was performed. The diagnosis was adenocarcinoma.

On December 10 his apical rate became quite irregular. An electrocardiogram revealed many premature auricular systoles. He received cedilanid-D 0.8 mg intramuscularly, followed by two doses of 0.4 mg at four-hour intervals. By evening the heart rate had become regular. An electrocardiogram the next day showed disappearance of the premature contractions.

Case 13. J. C., a 48-year-old female, had a known history of paroxysmal auricular tachycardia. She had been on maintenance digitalis and quinidine but had taken both medications irregularly. She was admitted to St. Vincent's Hospital on September 14, 1957 because of rapid heart action which had not responded to sedation. An electrocardiogram showed paroxysmal nodal tachycardia with ST changes of myocardial ischemia (Fig. 3C).

The patient was given 0.8 mg of cedilanid-D intravenously followed in two hours with another injection of 0.4 mg and repeated four hours later. An electrocardiogram the next morning showed normal sinus rhythm with first degree A-V block. The ST changes persisted for 48 hours more and then reverted to normal. It is possible that the A-V conduction defect represented early digitalis toxicity. She was discharged on maintenance dosage of oral digitalis.

*Comment:* These nine patients responded well to cedilanid-D. The only instance of even mild toxicity was that of the patient in case 13 who showed an A-V conduction time of 0.24 second. This returned to normal in 48 hours.

## Discussion

Paroxysmal auricular arrhythmias often may persist for days without seriously affecting the clinical condition of the patient. On the other hand, these arrhythmias may demand rapid emergency measures in certain cases, particularly in the elderly or debilitated, or in those people with underlying heart disease. It is in these urgent cases that rapidly acting digitalis preparations have been especially helpful.

Certain considerations must be kept in mind in the selection of the particular digitalis preparation to be used. Many of these patients may have already received digitalis prior to the present episode so that the possi-

bility of digitalis being the cause of the arrhythmias must be resolved. Again, the use of digitalis in a person already digitalized may present the problem of possible overdigitalization with toxicity and/or further disturbance of the cardiac rhythm. In emergencies it is frequently impossible to elicit information from the patients as to their previous use of digitalis, thus presenting a situation which taxes the clinical judgment of the attending physician. The usefulness and safety of lanatoside C under these conditions have been described by Ray and LaDue,[11] Harrison,[12] and Master *et al.*[1] This application has been extended recently to cedilanid-D by Sanazaro,[6] who reports that the therapeutic response or minor signs of toxicity provide effective end points for the probative use of cedilanid-D in determining the degree of digitalis saturation. Both of the above considerations demand the selection of a digitalis preparation with both rapid onset of action and rapid dissipation.

All of the 13 cases reported here attest to the rapid action of cedilanid-D and attainment of desired clinical effects without any clinical evidence of toxicity. This illustrates the wide margin of safety of this preparation, a factor which increases its clinical usefulness.

Much discussion has arisen over the conversion to another digitalis preparation for oral maintenance when any of the rapidly acting digitalis preparations has been used for emergency therapy. With the strophanthus preparations, the patient often will require complete redigitalization. However, our experience with cedilanid-D indicates that redigitalization is not necessary and that no difficulty is encountered in changing to the oral form of digitalis.

## Summary

Case histories of 13 patients who have received cedilanid-D by intravenous or intramuscular injection are presented. These show that this agent was effective in producing either rapid slowing of ventricular rate or conversion of various paroxysmal supraventricular arrhythmias to normal sinus rhythm. In most instances, the initial dose was 0.8 mg of cedilanid-D intravenously or intramuscularly followed at two- or four-hour intervals by 0.2–0.4 mg increments until a total of 1.6 mg had been administered. Beneficial effects without toxicity followed the use of cedilanid-D in several patients who had previously received digitalis. There were no signs of toxicity in any of the patients treated.

This study has shown that cedilanid-D is a safe and highly effective drug in the reduction of rapid ventricular rates in chronic auricular fibrillation and the conversion of paroxysmal auricular arrhythmias to normal sinus rhythm.

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# Review

# A-V Dissociation: A Reappraisal*

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ON COMPARING the accounts of interference-dissociation written by acknowledged exponents of the arrhythmias,[7,65,111] one is distressed and bemused to find anything but unity and concord. Indeed, the whole subject has long been clouded by a confused nomenclature, inconsistent usage, and defective definition. We have attempted to unravel the terminologic tangles by tracing the threads back to their first beginnings. In so doing the subject has been greatly clarified for us and we hope that a presentation of our researches may help to lessen the bewilderment of others.

Our second purpose is to examine and criticize existing definitions of interference-dissociation and to illustrate points of argument from a series of our own tracings. Third, we would make brief comment, based partly on our analysis of 10,000 consecutive tracings in a general hospital, on the incidence and significance of this arrhythmia.

Lest there be doubt that confusion and inconsistency exist even in high places, let us quote the following three examples: A recently published textbook of electrocardiography[47] describes interference-dissociation in the following words: "This is a complete A-V heart block in which the ventricular rhythm is irregular. The etiology, clinical significance, prognosis, and treatment are the same as for a complete heart block." In a leading heart journal, presumably with both authorial and editorial sanction, the running head of an article dealing with interference-dissociation reads "A-V block."[128] An author, apparently forgetful of his own former usage,[64] includes the following censorious footnote in a recent edition: "The term interference-dissociation applied loosely by others for this variety of A-V dissociation will not be used in this text."[65]

A recent detailed review of the subject,[88] the first in English since the classic paper by Zeisler[138] in 1932, is an excellent exposé of the intricacies of mechanisms, but does little to clarify nomenclature; indeed the authors introduce new terms, such as ipse-directional (sic)†, contradirectional, direct, delayed, isolated and repetitive interference, which tend to clothe the subject in further complexity.

## TERMINOLOGY

### (A) DISSOCIATION

The term A-V dissociation can, with justification, be applied to any situation where atria and ventricles are not controlled by a common pacemaker. But for practical purposes we are concerned only with those arrhythmias that are likely to be given A-V dissociation as their primary and identifying title. In ventricular tachycardia (without retrograde conduction) and in simultaneous atrial and nodal tachycardia, dissociation between atria and ventricles obviously exists; and "momentary"[138] dissociation may be said to occur in ventricular premature beats (without retrograde conduction), in main-stem extrasystoles, and in some single escape beats, nodal or ventricular. No one

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† This, moreover, is a bad coin. If ipse, *self*, must again be wrongly used to mean *same*, it should at least be compounded correctly from the stem of its genitive, i.e., ipsi-, from ipsius.

applies A-V dissociation, however, as a primary descriptive term to, say, ventricular extrasystoles or tachycardia, and therefore confusion does not arise. On the other hand many authorities, and especially European writers,[43,51,57,65,77,88,128] sanction use of the term to embrace both complete A-V block and interference-dissociation.

To apply the term A-V dissociation in a generic way to complete A-V block as well as to interference-dissociation is semantically acceptable and has much to recommend it; for words exist for their meaning alone and the meaning of dissociation in English, French, or German is perfectly clear and unambiguous. But in scientific jargon it is often expedient to limit the application of a word of general meaning to a specific sense—for example, complement—and there is a great deal to be said for limiting the use of A-V dissociation to the arrhythmia referred to above as interference-dissociation and illustrated in Figure 1. Many authorities now use the term in this restricted sense alone and for the purposes of our further discussion we shall so limit its usage.

For A-V dissociation to occur, atria and ventricles must fall out of step. This happens if the ventricular pacemaker beats before the atrial impulse arrives, either because the ventricular beat is early or because the atrial impulse is late. The usual mechanism is either that the sinus rate slows to a rate slower than the inherent rate of the A-V node, or that A-V nodal rhythmicity increases to a rate faster than the prevailing rate of the sinus node. In many cases both factors operate and the dissociation is due to a combination of sinus slowing with enhanced A-V excitability. Once the chambers have lost step, the pattern of the subsequent interplay of rhythms depends mainly on the relative rates of the two pacemakers. If their rates are sufficiently dissimilar, conducted beats from atria to ventricles will periodically occur (Fig. 1); if, on the other hand, the rates of the two pacemakers are similar, the opportunity for conducted beats will not arise (Fig. 4A).

When dissociation results from atrial slowing it is convenient to describe it as dissociation "by default," and when it results from increased A-V nodal or ventricular irritability as dissociation "by usurpation."[1,85] These mechanisms have also been referred to respectively as "passive" and "active heterotopy of the A-V center."[24]

Since the heart serves two masters, the situation was called "la double commande" by Geraudel,[42–44] and in a similar vein has been called "double rhythm" in English.[121] Some authors have used "ventricular escape" as synonymous with A-V dissociation.[51,67,131,132]

### (B) ESCAPE

Escape is a safety mechanism; it ensures that a lieutenant takes command when the captain falters. When the S-A node defaults, the inherent excitability of a lower pacemaker (usually the A-V node, but sometimes an ectopic ventricular focus) comes to the rescue and takes charge of the ventricles. The essential of an escaped beat is that it is *late;* it puts in its appearance only when an expected impulse fails to arrive on schedule. If a series of escaped beats ensues, A-V dissociation (by default) is the result.

Usage of the term escape has also been inconsistent. While many authorities properly reserve its use for the late "rescuing" beat,[1,5,7,35,46,65,79,91,110] others have embraced

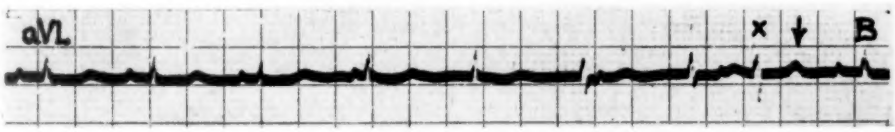


Fig. 1. Typical example of A-V dissociation from a 12-year-old girl with rheumatic fever. Ventricular capture occurs at *x*, thus disturbing the automatic ventricular rhythm with an early beat. If this capture beat had not occurred, the next automatic beat would have fallen after the usual R-R interval at the arrow. The capture beat, however, on its way through the A-V tissues discharged the impulse that would have initiated the next automatic beat at the arrow and so this beat is delayed to *B*. The capture beat thus doubly dislocates the automatic ventricular rhythm.

the mechanism of usurpation as well as that of default;[52,57,77,132] thus, according to White:[132]

> "Two types of such ventricular escape should be recognized: first, that which is dependent primarily on a depression of the pacemaker in the sinoauricular node; and second, that which is dependent primarily on an excitation of the pacemaker in the atrioventricular node."

He therefore classified A-V dissociation into two types, the "complete heart block type" and the "ventricular escape type," and he has continued to use ventricular escape synonymously with interference-dissociation in more recent writings.[51] Weller[128] on the other hand distinguishes ventricular escape from interference-dissociation by applying escape when the operative mechanism is default and by unjustifiably reserving interference-dissociation for the type of dissociation that results from usurpation.

Apart from spontaneous sinus slowing, referred to in the previous section as one of the usual mechanisms, any other event that delays the arrival of atrial impulses at the A-V junction may permit a lower pacemaker to assume control of the ventricles; such mechanisms include (1) S-A block, (2) A-V block with failure of an atrial impulse to reach and discharge the lower pacemaker, and (3) an extrasystole, by temporarily suppressing the S-A pacemaker.[98,111]

An extrasystole can also initiate A-V dissociation when the postextrasystolic pause is longer than the cycle of the automatic ventricular center. In this situation it is a moot point whether the mechanism should be considered default or usurpation. The first automatic beat after the extrasystole is late, inasmuch as it follows the extrasystole after a longer interval than the prevailing P-P interval; to this extent the mechanism may be considered default and the automatic beat an escaped beat. On the other hand there has been no failure of the sinus node to maintain its schedule and the event that sets the stage for the automatic rhythm to take over is a premature systole, itself a usurping mechanism; this provides the opportunity for the automatic center, itself often somewhat more excitable than normal, to discharge ahead of the next rhythmic sinus impulse. The aggregate, then, of the extrasystole plus the automatic beat may well be regarded as a usurping partnership.

### (c) INTERFERENCE

Whereas dissociation has been used as both a generic and specific term, interference has been given several differing senses, some of which are diametrically opposed and mutually exclusive. In order to facilitate description of its main usages it will be helpful to refer to an example of A-V dissociation. In Figure 1 atria and ventricles are beating independently with the sinus node in control of the atria while the A-V node controls the ventricles at a somewhat faster rate. The slower P wave therefore "overtakes" and passes the QRS complex. When the P wave falls far enough beyond the QRS so that the junctional tissues are no longer refractory, the atrial impulse is conducted to the ventricles ($x$). Thus a series of regular independent ventricular beats is interrupted by an early (conducted) beat. With reference to this example, let us now consider the four main usages of the term interference:

*Sense 1:* At its simplest, interference refers to the interruption of the otherwise regular beating of the ventricles by the conducted sinus impulse—the atrial rhythm "interferes" with the ventricular rhythm by producing an early beat.

*Sense 2:* This same disturbing impulse, however, interferes in a second way with the ventricular rhythm. For, by the time the conductible sinus impulse reaches the A-V node, the node has already begun to build up its next rhythmic impulse; this is discharged by the descending S-A impulse and therefore a new impulse must begin to form. The next A-V impulse is thereby delayed and activates the ventricles at B (Fig. 1) instead of at the arrow, which is where the next nodal beat would have occurred if the conducted atrial impulse had not interfered with its timetable.

(Note that in both these senses interference is vested in the *conducted beat alone.*)

*Sense 3:* On the other hand the term is used by some in the technical electrophysical sense, "the mutual extinction of two excitation

waves that meet in any portion of the heart."* The classic example of this form of interference is seen in a "fusion" or "summation" beat. A fusion beat can be seen in A-V dissociation only in two sets of circumstances: (a) a ventricular fusion beat may occur if the ventricles are under control of a low ectopic pacemaker rather than the A-V node; or (b) an atrial fusion beat will result if the nodal impulse begins to travel backwards into the atria before the sinus impulse has activated the whole atrial myocardium.

Theoretically, a similar collision of opposing impulses can occur in the junctional conducting tissues, so that a descending atrial impulse and a retrograde A-V (or ventricular) impulse meet and extinguish each other before the ascending impulse has reached the atrial myocardium. Such interference is electrocardiographically indistinguishable from that in sense 4 below.

*Sense 4:* When the A-V node discharges its impulse just before the sinus impulse arrives, the sinus impulse finds the A-V tissues refractory. The refractory junctional tissues thus interfere with the passage of the normal S-A impulse and it can be said that it is *because of* this type of interference that atria and ventricles remain dissociated.

(Note that in this sense interference is a property of *all beats except* the conducted beat, and is therefore confusingly opposed to senses 1 and 2 above.)

All of these usages are in themselves reasonable and acceptable, but confusion arises, and indeed is fostered, when authorities use interference in one or other sense exclusively and make no mention of the conflicting usage of others. In general, it may be said that authors group themselves into two opposing camps: those who use interference in one or both of the first two senses[3,7,15,19,25–27,34,35,55,108,111–113,115,138] and those who use the term in one or both of the last two senses.[5,41,62,63,65,88,89,121,133,134,136,139,140] It should be emphasized that the conflict arises because usages of the term fall into two basic categories: on the one hand interference indicates a disturbance of *cardiac rhythm* (as in senses 1 and 2 above), while on the other it refers to a disturbance in the spread of *electrical impulses* (as in senses 3 and 4). For convenience we shall continue to refer to the senses in which interference is used by the above numbers.

* *Blakiston's New Gould Medical Dictionary*, 1956.

### (D) THE CONDUCTED BEAT

The conducted beat that interrupts the automatic ventricular rhythm and momentarily brings the ventricles under atrial control has generally been referred to as an "interference beat" or a "ventricular capture." For those who use interference in its simpler senses only (senses 1 and 2), interference beat[3,7,15,35] is appropriate and adequate. But this term obviously cannot be employed by those who use interference in sense 4 because the conducted beat is the only beat that shows *no* interference of this type.

Ventricular capture (or "capture beat"), on the other hand, is widely used and can be applied regardless of the sense in which interference is used; furthermore "capture" has the virtue of having found acceptance in French,[43,73,94] Spanish,[6,18,41,93,95] and Italian[4] as well as in English; and in German, Wenckebach and Winterberg[130] borrow and quote the English "ventricular capture."

### (E) TERMINOLOGY IN THE LIGHT OF HISTORY

A-V dissociation was apparently first demonstrated by Cushny[20] in 1897 when he showed that digitalis, pushed to the point of intoxication in dogs, often produced this arrhythmia. In Cushny's words:

> "Accordingly we find the irritability of the ventricle at last so great that the slow auricular rhythm is no longer sufficient to satisfy it and the ventricle takes up its own rhythm, and is therefore now set in motion by two sets of impulses, one generated in its own, the other derived from the auricular muscle. As long as the extraneous impulse reaches the ventricle during its refractory period it will have no effect, and if the two rhythms are nearly equal a number of impulses are therefore ineffective. In this way the irregularity becomes periodic, the periods being longer at first when the rhythms are nearly equal, but becoming shorter as they diverge more from each other. . . . Thus we may have an interference occurring in the

ventricle from the clashing of the auricular and ventricular rhythms while the ventricular impulses are unable to pass to the auricle, and the latter therefore beats perfectly regularly."

Von Tabora[126] in 1906 again described the arrhythmia induced in dogs by digitalis but published no illustrative tracings. In 1910 Rothberger and Winterberg[103] recorded the arrhythmia in dogs with the electrocardiograph and in the same year Hewlett and Barringer[58] were able to say that digitalis-induced A-V dissociation "is so common in carefully graded digitalis poisoning in dogs that it has become a regular portion of the pharmacologic demonstration given by Dr. Edmonds to the University of Michigan students and Professor Hatcher to the Cornell University students. So far as we know this form of irregularity has never been described in man." They then recorded with mechanical records what they believed to be the first published clinical example, also probably digitalis-induced.

But they had overlooked a clinical record published by Wenckebach[129] in 1906, accompanied by this description of the phlebogram: "in the curve one sees how 'a' approaches 'c' and soon unites with it forming a tall wave. Then it appears later than 'c' and in the following systoles even later until finally it comes so late that an extrasystole follows. After the extrasystole 'a' is found again in its normal position before 'c'." His explanation of the disturbance, however, was at fault. It was clear from the phlebogram that the right atrium, producing the 'a' waves, was dissociated from the ventricles; and so, apparently unable to believe that the ventricles could beat without an atrial pacemaker, he invoked "longitudinal dissociation" between the atria and concluded that the *left* atrium controlled the ventricles while "the right atrium works on its own and its action interferes with the action of the rest of the heart."

In 1914 Weil[127] and Gallavardin and associates[38] published the first clinical electrocardiograms showing A-V dissociation. Gallavardin clearly appreciated the underlying mechanisms: "the two principal conditions that determine the appearance of this intermittent ventricular automatism are: (1) slowing of the auricular rhythm to beyond the idioventricular cycle; (2) acceleration of the idioventricular rhythm to less than the auricular cycle."

The first clinical examples in the English literature were published by Wilson[133,134] in 1915 and White[131] in 1916. Wilson called the phenomenon "complete atrioventricular dissociation" while White referred to it simply as "ventricular escape." Taschenberg[123] in 1921, like Gallavardin, used the term "ventricular automatism" and alluded to "dissociation and interference" between atria and ventricles.

In 1923 Mobitz[89] established this arrhythmia as an entity in its own right and gave it the name that has remained the common coin, *Interferenzdissoziation.* Mobitz believed that this form of dissociation was caused "by the way in which the sinus and A-V rhythms interfere with one another, and therefore it seems fitting to distinguish it as 'interference-dissociation'." Scherf[108] in 1926 renamed the disturbance *Dissoziation mit Interferenz:* "we prefer to call it 'dissociation with interference' since dissociation does not develop because of the interference but interference becomes possible because of the dissociation." Scherf used and uses[111] interference in senses 1 and 2.

In the following year, however, Wenckebach and Winterberg[130] subdivided examples of dissociation with interference into those with and those without "linkage of rhythms"; by linkage of rhythms they referred to the capture beat and this therefore suggests that, unlike Scherf, they did not necessarily regard interference as a function of the capture beat. For one of their types of dissociation with interference was dissociation without capture beats. In the same text they also use "incomplete dissociation" to describe dissociation with capture beats.

### (F) CONCLUSIONS CONCERNING TERMINOLOGY

Since their introduction the terms interference-dissociation and dissociation with interference have both been widely used. But they are not entirely satisfactory because, if interference is used in sense 1 or 2, it applies to the capture beat alone and therefore neither term can properly be applied to dissociation without capture beats.

Some authorities employ complete dissociation when there are no capture beats and incomplete dissociation when capture beats are present. But again this usage is not without objection, partly because of the long enjoyed attachment of the term complete A-V dissociation to complete A-V block; but especially because the degree of dissociation is certainly not increased—from incomplete to complete—by the absence of capture beats. Indeed it is often the more fleeting and less established examples of dissociation in which the opportunity for capture does not arise. Moreover, longer tracings of so-called complete dissociation will often reveal capture beats to be present.[7,88] This usage therefore tends to be misleading and is not conveniently analogous to the application of complete and incomplete to degrees of A-V block.

It is also regrettable that interference-dissociation has been applied to other arrhythmias. It has been erroneously used of the interaction of the two rhythms in simple ventricular parasystole[59] and it has also been applied to examples of almost complete A-V block in which occasional forward conduction takes place when the supraventricular impulse happens to arrive at the junctional tissues at a favorable time[14] (usually attributed to the supernormal recovery phase).[14,15,60,78,83,96,137] It would seem preferable to reserve Mobitz' term for the context in which he used it. If it were permissible to use interference-dissociation for any disturbance of rhythm in which the regular operation of one rhythm is periodically interrupted by an early beat originating in a second independently beating pacemaker, then it would be even more properly applied to the occasional retrograde conduction of an impulse from the ventricles into the atria during complete A-V block (atrial capture); for this is more closely analogous to the interference-dissociation of Mobitz than is complete A-V block with fortuitous forward conduction. Indeed it has been well characterized as "interference-dissociation between ventricle and auricle"[136] and as "dissociation with interference in reverse."[25]

In view of the prevailing confusion, in the interest of simplicity without ambiguity, and to avoid the introduction of unnecessary new terms, we would suggest that the simplest nomenclature would reserve A-V dissociation for the arrhythmia we have been discussing and that it would be simply subdivided into: (1) A-V dissociation with capture beats and (2) A-V dissociation without capture beats. Under the second heading we would add that isorhythmic dissociation, introduced by French authors,[31,101,119] is an apt term that can be applied to long or short runs of dissociation between pacemakers having equal rates; and that, if such dissociation is prolonged and there is reason to suspect the operation of synchronization,[118] dissociation with synchronization or synchronized dissociation[116] may be suitable.

Finally we would suggest that when complete A V block is meant, complete A-V block be said and the term A-V dissociation be eschewed.

### Definition of A-V Dissociation

From a study of available definitions of A-V dissociation it may be fairly said that most of the following terms are often either stated or implied:[5,7,35,91] that atria, under control of the S-A node, and ventricles, under A-V nodal control, beat independently with ventricles beating faster than atria; and that, while retrograde block protects the atria from control by the faster beating ventricles, forward conduction remains unimpaired. These criteria not uncommonly hold true; however, we have been impressed by the frequent occurrence of exceptions and, from the analysis of our tracings in the final section of this paper, it will be evident that exceptions are indeed commonplace.

As constituents of a definition, therefore, the terms outlined above are found wanting. For definitions, although they should be as brief as possible, should be inclusive and embrace all varieties of the thing defined. The purpose of defining is to set the limits within which all examples of the thing defined will fall and outside which everything else will lie. To require accurate definition is not pedantic; on the contrary, anything less than Socratean insistence on a clear preliminary definition of terms is indefensible in any science. It is our purpose to point out that existing definitions of A-V dis-

sociation are too narrow and that indeed not one of the above criteria is essential to its diagnosis. To this end we shall approach each criterion in turn.

(a) *Atria Are Not Necessarily Under Sinus Control:* For dissociation between atria and ventricles to occur, it is clearly not essential that the atria should remain under control of the normal sinus pacemaker. An example of A-V dissociation with atria under ectopic (? coronary sinus) control is shown in Figure 2A. Clear examples have been published by Luten and Jensen[82] and by Schott.[113] Another tracing, published as an example of reciprocal rhythm,[2] is more readily explained as A-V dissociation with ectopic atrial control.

(b) *Ventricles Are Not Necessarily Under A-V Nodal Control:* Similarly there is nothing in the mechanism of A-V dissociation that makes it necessary for the ventricles to be under control of the A-V node rather than an ectopic ventricular pacemaker. An ectopic focus may be more excitable than the A-V node and may assume control either by usurpation or when the sinus node defaults. Ventricular usurpation, at its most dramatic, is seen in ventricular tachycardia; here the drama of the tachycardia overshadows the fact of dissociation, but the fundamental mechanism is similar to A-V dissociation at more modest ventricular rates.[26,65] An example of A-V dissociation with ectopic ventricular control developing as a result of sinus slowing is shown in Fig. 2B and excellent examples have been published by Dressler,[27] Magri,[84] Scherf and Boyd,[110] and Miller and Sharrett.[88]

If ventricular complexes prior to the development of A-V dissociation are not available for examination it will be impossible to distinguish between an ectopic ventricular pacemaker and a nodal pacemaker with concomitant intraventricular block. In these circumstances one can only be certain that an ectopic focus is controlling the ventricles if capture beats occur which show normal intraventricular conduction or at least fusion beats (Fig. 3A). Dressler[26] has emphasized that this same phenomenon is useful in distinguishing ventricular tachycardia from supraventricular tachycardia with associated intraventricular block (Fig. 3B). If,

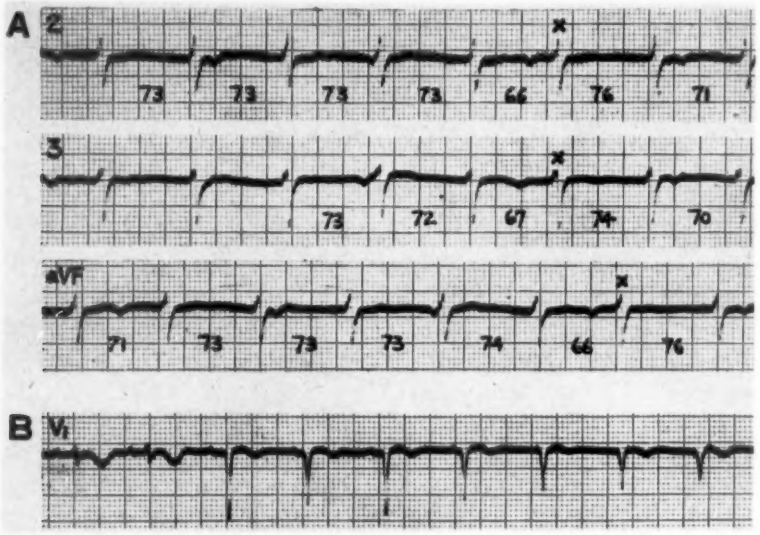


Fig. 2. (A) From a 71-year-old man with coronary disease who was receiving digitalis. R-R intervals are indicated in hundredths of a second. Atrial rate 48, ventricular rate 84. P waves are inverted in leads 2, 3, and aVF, indicating ectopic atrial control. In each lead the shorter R-R intervals are terminated by ventricular captures. These capture beats (*x*) show the same QRS pattern as the automatic ventricular beats and therefore indicate that ventricles are under nodal control. (B) From a 6-year-old boy with rheumatic fever. The first two beats are conducted sinus beats. Then, as a result of sinus slowing, the ventricles escape under control of an ectopic ventricular focus as indicated by the changed QRS pattern. Dissociation continues to the end of the strip.

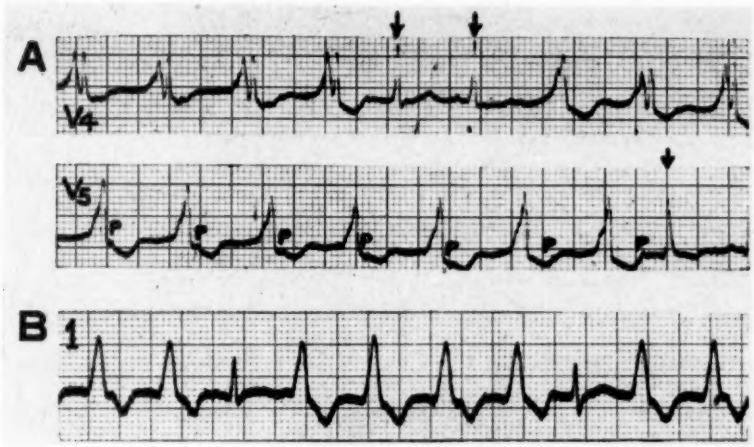


Fig. 3. (A) From a 58-year-old man with diabetes and recent myocardial infarction. Ventricular rate 110, with ventricles under ectopic control except for capture beats (arrows) which show relatively normal intraventricular conduction. (B) From a 46-year-old man with recent myocardial infarction. Relatively slow ventricular tachycardia (rate 130) with occasional capture beats showing normal intraventricular conduction.

on the other hand, capture beats are seen to exhibit the same prolonged and bizarre configuration as the automatic beats, this is evidence, as Langendorff[71] points out, that the ventricles are under nodal control with associated intraventricular block.

(c) *Atria and Ventricles Are Not Always Entirely Independent:* Wenckebach and Winterberg[130] stated that the atrial and ventricular rhythms were "linked" only by the capture beats. However, during dissociation, more or less prolonged stretches of synchronous beating between atria and ventricles may occur and these are unlikely to be fortuitous. They are probably explained by the phenomenon of synchronization, so clearly documented by Segers[118] who called the shorter stretches *accrochage*. We have recently reviewed this subject in detail.[116]

(d) *Ventricles Do Not Always Beat Faster Than Atria:* Although it is true that dissociation is generally initiated either by the atrial

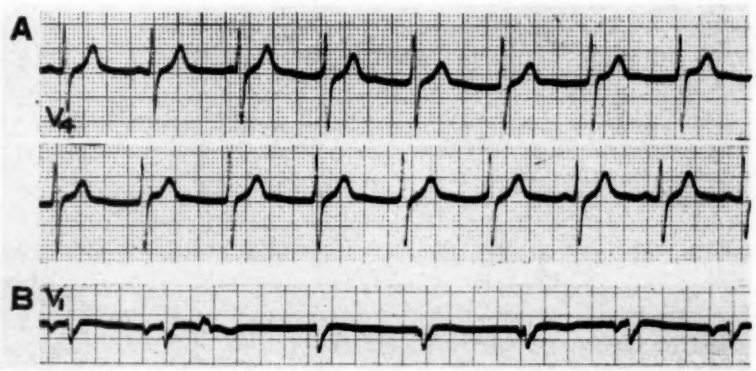


Fig. 4. (A) A-V dissociation without capture beats, from a 62-year-old man with prostatic hypertrophy but no evidence of cardiac disease. The two strips form a continuous tracing. In the upper strip atria are slower than ventricles and P waves therefore overtake and pass the QRS complexes. In the lower strip, however, the P waves return through the QRS to their former position. Throughout the lower strip, therefore, atria are beating slightly faster than ventricles, but dissociation is just as real as in the upper strip. (B) From a 56-year-old man with recent myocardial infarction who was receiving digitalis. The first two beats are conducted sinus beats. The third beat, a premature ventricular beat, temporarily suppresses the S-A node. As a result the ventricles begin to beat automatically under nodal control until the S-A node regains control for the final beat. During the whole brief four-beat bout of dissociation, atria are beating faster than ventricles.

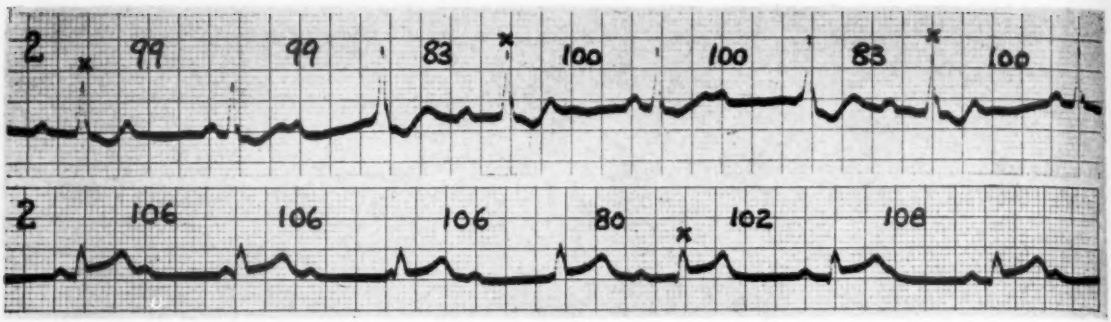


Fig. 5. A-V dissociation in the presence of 2 to 1 A-V block. R-R intervals are indicated in hundredths of a second and the shorter intervals are terminated by conducted beats (*x*). The upper strip is from a 39-year-old woman with malignant hypertension and uremia who was receiving digitalis. The automatic ventricular rate is 60, whereas the conductible atrial rate (the atrial "half-rate") is 53–54. The lower strip is from a 60-year-old woman with recent myocardial infarction. The automatic ventricular rate is 57, while the atrial half-rate is 54.

pacemaker slowing to a rate below the inherent rate of the ventricular pacemaker or by the ventricular pacemaker accelerating to a rate above that of the atria; yet it is not true to state unreservedly that during A-V dissociation the ventricles beat faster than the atria. As a matter of fact, in transient bouts of dissociation set off by an extrasystole, during the entire brief period of dissociation the atria may be beating faster than the ventricles (Fig. 4B); and in many longer periods of isorhythmic dissociation it is obvious that there are often stretches during which the atria are beating slightly faster than the ventricles (Fig. 4A).

Then there are those examples of A-V dissociation in which the dissociation is superimposed on a background of 2 to 1 A-V block. Mobitz described this phenomenon[89] and subsequent excellent examples have been published by Dressler,[23,25,27] Schott,[114] and Magri;[84] further examples are shown in Figure 5. In these tracings, although the ventricular rate is not faster than the atrial, it is faster than the rate of *conductible* atrial impulses. This may be symbolically expressed (where $V$ = ventricular rate and $A$ = atrial rate) as $V > A/2$.

We have seen that one of the mechanisms whereby dissociation develops is default of the atrial impulse, as when sinus bradycardia causes the atrial cycle to lengthen beyond the escape interval of the ventricular pacemaker. Now from the point of view of the ventricle, the atrium defaults whenever its impulse fails to arrive on schedule; and this schedule can be interrupted as well by A-V block as it can by sinus bradycardia or sinus block. In sinus bradycardia or block the impulse fails to form (or at least to leave the S-A node), in A-V block it fails to arrive. The effect, so far as the ventricle is concerned, is the same.

Thus in 2 to 1 A-V block, if the ventricles' escape interval is shorter than *two* atrial cycles, ventricular escape will occur; in other words the 2 to 1 A-V block makes the rate of conductible atrial impulses slower than the automatic ventricular rhythm. Criteria for recognizing this situation have been well laid down by Dressler[27] and Magri.[84]

Katz[63] published several such tracings as "almost complete A-V block." Analysis of these records suggests that A-V dissociation in the presence of 2 to 1 A-V block is a more likely explanation. Berman[8] has confused the situation further by publishing several similar tracings under the heading of "reverse Wenckebach periods" despite the fact that similar terms have been previously applied to a different and more appropriate mechanism.[9,28] Berman's records are more readily interpretable as A-V dissociation in the presence of 2 to 1 A-V block though he does not consider this possibility in his discussion.

In conclusion it should be pointed out that when, in the presence of incomplete A-V block, the respective rates of the two pacemakers are unfavorably adjusted so that the critical R-P time plus A-V conduction time is longer than the ventricular escape interval, no beats at

all will be conducted to the ventricles and complete A-V block will be perfectly simulated.[27] The absence of forward conduction, therefore, is not necessarily evidence of complete A-V block. Further, one should add that rarely complete A-V block can present an atrial rate that is slower than the ventricular.[76] The relative rates of atria and ventricles, therefore, as emphasized by Miller and Sharrett,[88] do not provide a reliable criterion for the differentiation of A-V dissociation from complete A-V block.

(e) *Forward Conduction Is Not Necessarily Unimpaired:* From the preceding paragraphs it is clear that A-V dissociation can accompany high grades of A-V block. Apart from such examples of 2 to 1 block, there is no question that some lesser degree of impaired conduction is often an accompaniment of A-V dissociation. Korth and Schrumpf[69] emphasized that forward conduction was not necessarily normal in the presence of dissociation and the close relationship of the prolonged P-R interval and A-V dissociation in rheumatic fever has been repeatedly noted.[50,72] This relationship has been accounted for in two ways: Grant[50] has postulated that the prolonged P-R interval and A-V dissociation are stable and unstable manifestations respectively of the same A-V defect, while Miller and Sharrett[88] have pointed out that, in accordance with their concept of the "zone of potential interference," prolonged A-V conduction time favors the development of dissociation.

The fact that the P-R interval of the capture beat is often prolonged, even when this beat is not particularly early, illustrates the presence of impaired A-V conduction. In Figure 6A the P-R interval of the conducted beat is 0.35 sec while the R-R interval corresponds to a ventricular rate of 94. Normal conducting tissues should surely do better than that even when taken slightly by surprise.

Further evidence of impaired forward conduction is afforded by examples of concealed conduction.[70] In this situation the atrial impulse is conducted far enough into the A-V tissues to discharge the forming A-V impulse, but is then blocked lower down and so prevented from activating the ventricles. But because the forming A-V impulse has been discharged, the next automatic ventricular beat is delayed (Fig. 6B) and this delay alone reveals the fact of part-way conduction. Others have styled this phenomenon "double interference" or "ladder type interference."[41,140]

Forward conduction, therefore, far from always being normal, is often impaired. On the other hand it must always remain possible,

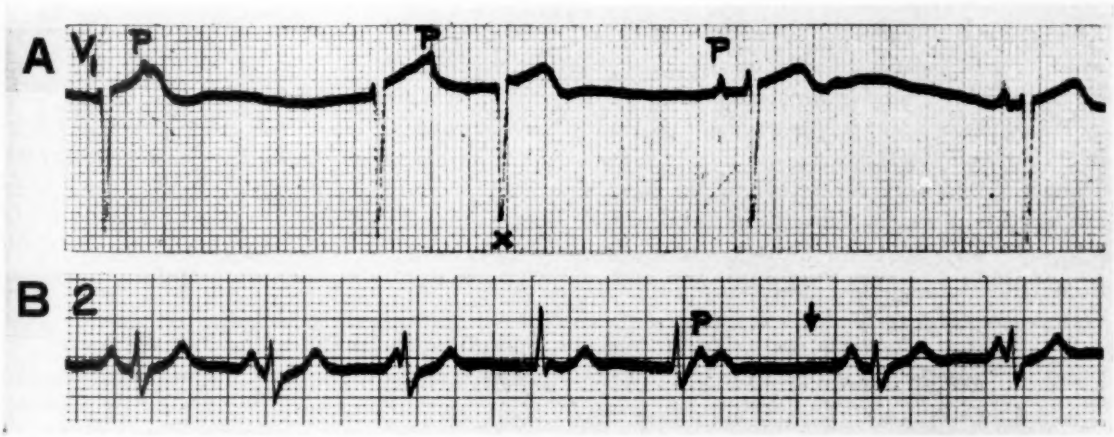


Fig. 6. (A) A few beats from a tracing showing A-V dissociation. The third QRS is a capture beat with P-R interval of 0.35 sec terminating an R-R interval of 0.64 sec. (B) A-V dissociation with concealed conduction, from the same patient as Fig. 4A. If the automatic ventricular rhythm had continued to be regular, the sixth beat would have appeared at the arrow after the usual R-R interval. It did not put in an appearance because the impulse of the labeled P wave penetrated into the junctional tissues and discharged the forming automatic impulse (which would have led to ventricular activation at the arrow) but was unable to proceed and activate the ventricles because it was blocked lower down. The concealed conduction is thus recognized by its delaying effect on the next cycle.

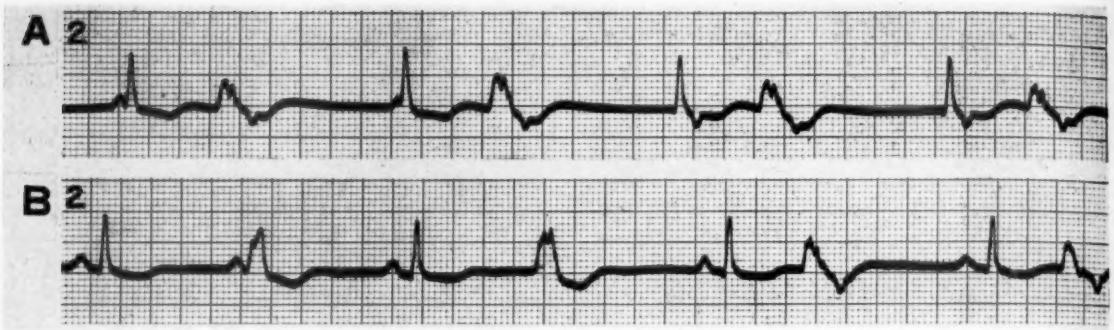


Fig. 7. From a 69-year-old man with hypertensive heart disease who was receiving digitalis. (A) Four couplets of bigeminal rhythm; the first beat of each pair is a supraventricular beat and the coupled beat is a ventricular extrasystole. All four extrasystoles show retrograde conduction to the atria (inverted P waves deforming S-T segments). The first two supraventricular beats show dissociation whereas the last two show retrograde conduction. This illustrates that dissociation is possible in the obvious absence of retrograde block. The R-P interval of the supraventricular beats is 0.12 sec, whereas that of the extrasystoles is 0.21 sec. (B) The extrasystolic beats show a sequential relationship to the P waves similar to that seen in the supraventricular beats in A. The first ectopic beat is an "end-diastolic" extrasystole occurring after the rhythmic P wave. The next extrasystole is earlier and the P wave is lost within it; the third and fourth ectopic beats are much more premature so that retrograde conduction is possible into the not yet activated atria. These two strips illustrate the presence and absence of retrograde conduction conditioned by time relationships alone.

otherwise the prevailing arrhythmia becomes complete A-V block by definition.

(f) *Retrograde Block Is Not Necessarily Absolute:* It is commonly stated that retrograde protective block is a sine qua non of A-V dissociation; if there were not such block, it is argued, the faster beating A-V node would take command of the entire heart. This appears logical, but it should not be accepted prima facie and without question; for the mere absence of retrograde conduction does not prove the presence of retrograde block. It is interesting to note that Mobitz[89] was unwilling to accept the concept of unidirectional retrograde block and unconvincingly suggested that the nodal impulse itself might be too "weak" to penetrate backward, yet be strong enough to travel downwards along its accustomed paths; or that there might be a differential "responsiveness" of the tissues above and below so that the nodal impulse found it relatively easy to travel downstream but more difficult to go upstream.

In considering the concept of retrograde block, there are three points to which attention should be drawn: first, if such block exists, it is hard to understand why it should at times switch itself on and off with such whimsy. For this indeed must happen in those cases where A-V dissociation and A-V nodal rhythm alternate. In such circumstances, as in Figure 7 and in tracings published by Burchell,[15] Gallavardin and Gravier,[39] Geraudel,[44] Jones and White,[61] and Miller and Sharrett,[88] retrograde conduction must be readily accomplished in one beat yet be completely blocked in the adjacent beat. The tissues that thus block and unblock themselves according to their fancy may well be likened, in Pickering's simile, to "whimsical children (as children were understood before contemporary psychiatry)."*

Second, an identical absence of retrograde conduction has in other circumstances been regarded as evidence, not of retrograde block, but of impulse formation at a lower point than the A-V node itself, namely in the main stem of the bundle of His.[87] Indeed, the recognition of a main-stem extrasystole has always depended on the assumption that lack of retrograde conduction into the atria is evidence that the impulse has a lower origin than the A-V node itself. Now the first dissociated cycle in A-V dissociation and a main-stem extrasystole may be electrocardiographically identical: in each a normal sinus P wave may be seen in relation to an independent but normal QRS; yet in the one case the absence of backward conduction is attributed to protective retrograde block

* *Lancet* 2: 845, 1951.

while in the other it is attributed to impulse formation at a lower level.

If this assumption of main-stem origin were valid, we might justifiably conclude that the factor determining whether A-V nodal rhythm or A-V dissociation develops, when a lower center escapes or usurps, is the site of impulse formation rather than the absence or presence of retrograde block. But this whole concept—that site of impulse formation determines retrograde conduction—may well be challenged in view of the fact that retrograde conduction is shown to be a common phenomenon even from low ventricular foci.[68]

Third, there are some cases of A-V dissociation in which we need assume neither retrograde block nor a lower-than-nodal pacemaker. From the not uncommon occurrence of post-incident P waves in A-V nodal rhythm (often conveniently referred to as "lower" nodal rhythm) it is clear that it sometimes takes longer for the A-V impulse to reach the atria than to reach the ventricles. If then in A-V rhythm the impulse may be tardy in reaching the atria, it becomes obvious that the sinus impulse may enjoy sufficient time to activate the atria completely before the ascending nodal impulse arrives, even if the sinus impulse is initiated somewhat later than the A-V impulse. It is thus possible that sinus P waves, even appearing as late as shortly after the QRS, could make their appearance without benefit of protective block. Miller and Sharrett[88] have designated the period during which the sinus impulse can control the atria without interruption from an ascending A-V impulse as the "zone of potential interference."

This affords a plausible explanation for certain examples of isorhythmic dissociation wherein the P wave does not wander far beyond the QRS. While it does not exclude the possibility of retrograde block, it certainly excludes the need for postulating such block as an inevitable attribute of every example of A-V dissociation. On the other hand, in A-V dissociation with capture beats, where the atrial rate is decisively slower than the ventricular and the P wave consequently marches across the R-R interval to effect ventricular capture, it is necessary to assume the presence of some protective mechanism that shelters the atria from nodal (or ventricular) control and discourages the lower impulse, now forming well ahead of the atrial impulse, from travelling backwards into the not yet activated atria. When there is no such discouragement, A-V dissociation switches—perhaps with a transitional atrial fusion beat or two—to A-V nodal rhythm.

In concluding we should make it clear that by block we mean an *abnormal* depression of conduction. To be sure, in a dissociated beat the sinus impulse cannot penetrate the A-V tissues because it has been anticipated by the nodal discharge, and the nodal impulse cannot enter the atria because they have been rendered refractory by the depolarizing sinus impulse; the passage of each into the other's territory is barred by refractory tissue, but this normal refractoriness following activation is not an abnormal depression. Unfortunately it has been called "secondary" or "adventitious" block;[88,138] if indeed it requires a name, it is better referred to as "physiologic interference"[65] (sense 4).

(g) *The Horse and the Cart:* Let us digress for a moment to examine the significance of the "zone of potential interference" and related

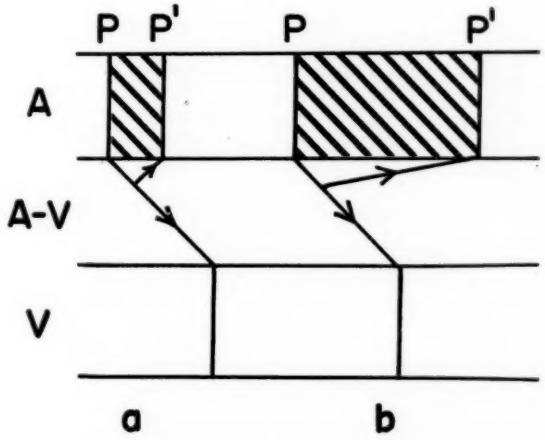


Fig. 8. Superimposed patterns of forward and retrograde conduction in two hypothetical hearts, a and b, in which conduction in each direction is possible. Forward conduction is represented as the same (0.16 sec) in both a and b. In a, retrograde conduction is rapid so that the P-R interval is 0.08 sec; in b, retrograde conduction is slower producing an R-P interval of 0.12 sec. The resulting zones of potential dissociation are shaded: in a, the zone is 0.16 − 0.08 = 0.08 sec; in b, it is nearly four times as long (0.16 + 0.12 = 0.28 sec).

TABLE I
Various Mechanisms of A-V Dissociation

| | Group I (Single beats) | Group II (A-V dissociation) | Group III (Tachycardia) |
|---|---|---|---|
| A. Usurpation | Ventricular extrasystole | →A-V dissociation with ectopic ventricular control | →Ventricular tachycardia |
| | Main-stem extrasystole | →A-V dissociation with nodal control of ventricles | →Nodal tachycardia without retrograde conduction |
| B. Escape | Ventricular escape | →A-V dissociation with ectopic ventricular control | |
| | Nodal escape | →A-V dissociation with nodal control of ventricles | |

matters. This "zone" is composed of the sum of forward and retrograde conduction times (Fig. 8) and obviously an increase in either will improve the opportunity for dissociation to occur. Where retrograde conduction is possible, dissociation can be initiated only when a sinus beat arises during this period; if it arises later, A-V nodal rhythm will result. In our opinion, therefore, this zone would more aptly be called the "zone (or period) of potential *dissociation*" which would lay emphasis on the horse rather than the cart. For, let us repeat, "the dissociation does not develop because of the interference, but interference becomes possible because of the dissociation."[108] Scherf here uses interference in senses 1 and 2, but his words are à propos no matter which meaning we give to the term; for although interference in sense 4 may be said to perpetuate dissociation, in whatever sense it is used it cannot be said to initiate it.

This is opposed to Katz' view. He has consistently maintained[62,63,65] that in nodal escape and in A-V dissociation "the impulses from the two pacemakers meet and obliterate each other by interference. . . In this way the independence of the two sets of chambers is *brought about*" (our italics).

This does not appear to us to be an accurate representation of the actual order of events. It is rather the getting-out-of-step, either because the atrial pacemaker lags behind or because the ventricular pacemaker hurries ahead (or because of other mechanisms previously mentioned), that initiates the dissociation and makes interference between the *already dissociated* pacemakers possible.

In considering this argument, let us refer to Table I in which group I represents the building bricks of which the arrhythmias in groups II and III are made. The point at which the basic disturbance in group I becomes the corresponding form of A-V dissociation (group II) is a matter of number; group III, on the other hand, is separated from group II on the basis of rate.

If an A-V focus usurps (without retrograde conduction) for a single beat, we call it, rightly or wrongly, a main-stem extrasystole; if a series of such beats occurs we have A-V dissociation. Again, if a low ventricular focus usurps for a single beat, we call it a ventricular premature beat; if a series of such beats occurs at a modest rate we call it A-V dissociation; if such beats develop at a rapid rate we call it ventricular tachycardia. Similarly, we may have one escape beat from either an A-V or a low ventricular focus, or we may have a series of escaped beats constituting A-V dissociation by default. The disturbances in group II (A-V dissociation) thus merge imperceptibly on the one hand with the members of group I and on the other with members of group III; for it has not been defined how many consecutive extrasystoles or escape beats are needed to justify the term dissociation; nor how fast the usurping rate may be before it must be called tachycardia rather than dissociation, though Pick[98] seems to suggest that 120 is the ceiling for dissociation by usurpation.

One cannot say that any of the disturbances in group I (single extrasystoles or escape beats) are produced by or are due to interference. Ergo, it cannot be said that the arrhythmias of which they are the *materia prima* are due to interference. It is because of the dysrhythmic initiative of a pacemaker that interference (sense 4) becomes possible.

(h) *Conclusions Concerning Definition:* In attempting to outline a working definition of A-V dissociation, we have arbitrarily elected three as the minimal number of consecutive beats necessary to justify the term, and, in accordance with the nomenclature of the New York Heart Association,[91] we have used a rate of 150 as the lower limit for ventricular tachycardia. This represents a wide, but we believe not unreasonable, embracement by the term A-V dissociation.

With all the many foregoing considerations in mind we suggest that a definition of A-V dissociation should go something like this: A disturbance of the normal A-V sequence in which, because of depression of the atrial pacemaker or excitability of the ventricular pacemaker, or because of both, atria and ventricles lose step and beat each in response to their own pacemaker for at least three consecutive ventricular cycles at a rate less than 150. This double autonomy is not the result of complete A-V block for, although some degree of incomplete block often coexists, forward conduction always remains possible and, when time relationships are favorable, the atrial pacemaker may regain control of the entire heart (ventricular capture) for one or more beats.

It should be noted that this definition makes no reference to the relative rates of the atria and ventricles; it does not specify what pacemakers must control the chambers; and it makes no specifications regarding independence or retrograde block. It also avoids use of the term interference, not because interference is in any sense a bad term, but because it has been so sinned against that the confusion attendant on its use can only be avoided by ignoring it.

## Incidence and Significance

Although A-V dissociation is most commonly seen and has most frequently been reported in rheumatic fever, coronary disease, and digitalis intoxication, it is important to emphasize that it can be a virtually normal finding. Unfortunately some of the sinister significance of complete A-V block has unjustifiably become attached to it; this is no doubt because both disturbances have been embraced by the term dissociation and confusion between the two is not uncommon, from time to time occurring even in print.[47,128] A-V dissociation, however, has resulted from a remarkable variety of autonomic influences which do not necessarily imply cardiac involvement; these include forced inspiration,[99] ocular pressure,[38] atropine,[38,57,131,134] atropine with adrenaline,[49] carotid sinus sensitivity,[131] increased intracranial pressure,[116] and pheochromocytoma.[16,32,53] It has apparently resulted from digital pressure over the precordium.[49] Salicylates, quinidine, and Pronestyl have produced it[65] and it has been associated with the administration of protoveratrine.[85] It sometimes complicates acute infections such as diphtheria,[100] scarlet fever,[115] pneumonia[21] and typhus.[139] In general, it may be said that when the arrhythmia results from sinus default it may well be benign, whereas when it results from nodal usurpation it usually represents pathologic excitability of the A-V node.

A-V dissociation is not a rare arrhythmia. Katz and Pick[65] report 681 examples among about 100,000 tracings, an incidence of 0.68 per cent or one example in every 147 tracings. Among 10,000 consecutive tracings interpreted by one of us at the Mercy Hospital, we have encountered 48 examples, giving an incidence of 0.48 per cent or one in every 208 records. These represent unusually high rates of occurrence, but in assessing the relative frequency of an arrhythmia one should bear in mind that its incidence will be higher when the electrocardiographer is interested in arrhythmias and when long strips are taken by technicians trained and encouraged to recognize disturbances of rhythm. Reported frequency will also be influenced by the arrhythmic variants included under the heading of A-V dissociation because its boundaries have never been clearly and satisfactorily defined.

On the basis of our attempted definition, we

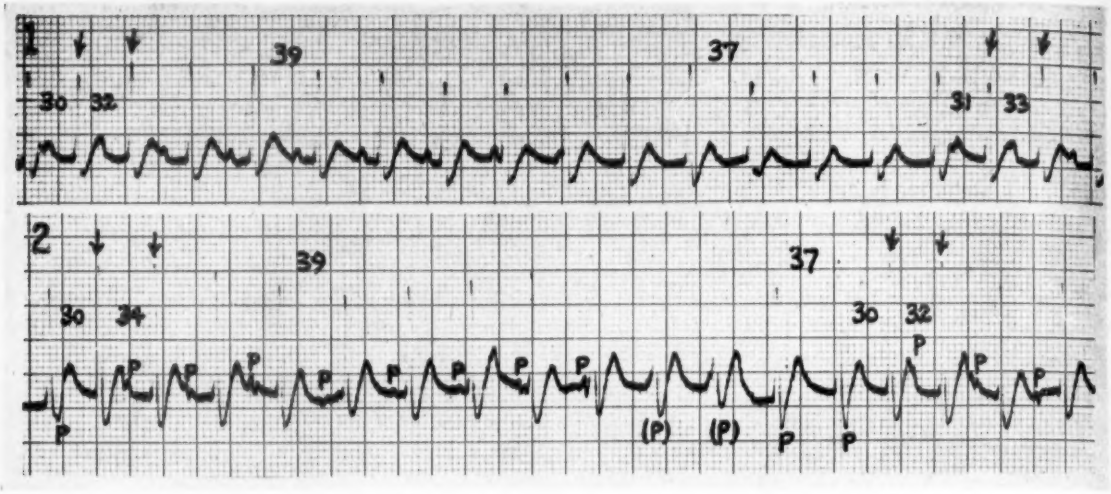


Fig. 9. A-V dissociation at high rates, with ventricular captures occurring in pairs, from a 56-year-old woman with thyrotoxic heart disease who was receiving digitalis. Atria are probably under ectopic control (diphasic P waves in lead 2) at rate 156; ventricles are under nodal control at rate 165. Several R-R intervals are indicated in hundredths of a second, and capture beats terminating the shorter intervals are indicated by arrows. All R-R intervals falling between pairs of capture beats measure 37 to 39 hundredths of a second.

have elected to include in our series examples showing three or more consecutive dissociated beats; this minimal criterion has in fact involved the inclusion of four examples, one from each of four patients. We have likewise included seven examples of usurping A-V or ectopic ventricular rhythms, at rates between 110 and 150, all of which show capture beats. We have also chosen to include, although the ventricular rate exceeds the limit laid down above, one example of simultaneous dissociated atrial and nodal tachycardia in which the sequence of 11 to 13 dissociated cycles followed by paired capture beats was regularly repeated (Fig. 9).

Our 48 examples were derived from 39 patients. Of these, five were over 70, 18 were over 60, and 30 were over 50 years of age. Of the nine patients under 50 years, six had unequivocal evidence of heart disease.

We have divided the tracings into those with transient and those with prolonged dissociation. On this basis 18 examples, derived from 14 patients, were classified as transient (showing only six or less consecutive dissociated cycles) but 13 of these 18 tracings contained repeated bouts of such transient dissociation. Prolonged dissociation was found in 30 records from 26 patients. Of these 30 tracings, 15 (including five with ventricular rates over 100) presented the classic pattern of repeated sequences of P waves "overtaking" the QRS with subsequent capture beats. Four further tracings derived from one patient showed no discernible P waves but frequent presumed capture beats (Fig. 3B). All four of these records presented a ventricular rate between 112 and 136 from an ectopic focus and might well be classified as slow ventricular tachycardia. Five examples were isorhythmic with no capture beats; five showed A-V dissociation in the presence of 2 to 1 A-V block; and one example, resulting from 2 to 1 S-A block, showed repetitive pseudoreciprocal rhythm or, as we think it is preferably called, "escape-capture bigeminy."[13]

Among the 39 patients, seven showed ectopic atrial and five ectopic ventricular control; three showed nodal control of the ventricles with associated bundle branch block. Eight of our series of 30 tracings of prolonged dissociation showed stretches of possible or probable accrochage or synchronization. Four of the 39 patients displayed A-V nodal rhythm with manifest retrograde conduction in sequence with A-V dissociation.

Of our total of 39 patients, only six had no demonstrable primary cardiac disease. Of these six, three were aged 62, 63, and 64 years,

respectively; one had inoperable carcinoma of the lung, one was admitted for benign prostatic hypertrophy, and the third had pulmonary tuberculosis, multiple myeloma, and severe anemia (Hb 8.9 g) with clinical, electrocardiographic, and radiologic evidence of left ventricular enlargement. Of the remaining three, two were aged 39 years; one of these was admitted with salicylate intoxication and the other was an alcoholic with aspiration pneumonia. The sixth in this group was 21 years of age and had a subarachnoid hemorrhage.

Of the remaining 33 patients with obvious cardiovascular disease, 26 had evidence of coronary disease, hypertension, or both; of these, 11 were suffering from acute myocardial infarction at the time the arrhythmia developed. Of the remaining seven patients with evident heart disease, three had chronic rheumatic disease, two had acute rheumatic fever, and one each had syphilitic and thyrotoxic heart disease. Of the 33 patients, 20 were receiving digitalis, but intoxication was clinically regarded as likely or possible in only seven. None were receiving quinidine, Pronestyl, or salicylates at the time A-V dissociation was recorded.

It is clear that in this series, consisting almost exclusively of in-patients in a general hospital, A-V dissociation was predominantly seen among the elderly with severe degenerative cardiovascular disease. Moreover, in acute rheumatic fever, dissociation may be the sole convincing sign of carditis and as such may assume the dignity of a "major criterion." We therefore cannot agree with the sweeping statement that "it is essentially a benign disorder. . .of no great diagnostic or prognostic importance."[88]

## Summary

(1) Attention is drawn to regrettable inconsistencies in usage of the terms dissociation, escape, and interference. The senses in which interference has been mainly used are detailed and discussed.

(2) The early history of A-V dissociation (interference-dissociation) is traced, especially as it exemplifies usage of the terms dissociation and interference. In the interest of clarity it is urged that A-V dissociation be reserved for this arrhythmia and be not applied to complete A-V block. By so reserving it, and by eschewing the maltreated term interference, much of the existing terminologic confusion could be avoided.

(3) Reasons are given for regarding interference-dissociation, dissociation with interference, complete dissociation, and incomplete dissociation as now unsatisfactory terms. It is recommended that A-V dissociation be simply divided into dissociation with and dissociation without ventricular capture.

(4) None of the six criteria often regarded as characteristic of A-V dissociation (sinus control of atria, nodal control of ventricles, independence between atria and ventricles, ventricles beating faster than atria, presence of retrograde block, normal forward conduction) is essential to the definition of this arrhythmia; indeed, exceptions to these terms are numerous. Such exceptions are illustrated and discussed and an attempt is made to redefine A-V dissociation.

(5) Interference (in one sense) is sometimes regarded as the cause of dissociation. It can be argued, however, that the principium of dissociation is not interference (in any sense); rather the original sin is the dysrhythmic whim of a truant (defaulting) or insubordinate (usurping) pacemaker.

(6) The incidence and significance of A-V dissociation is briefly commented upon. In a series of 10,000 consecutive tracings in a general hospital, this arrhythmia was diagnosed 48 times (0.48 per cent or one in every 208 records). It occurred mainly in elderly patients with severe degenerative cardiovascular disease.

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# Franz Groedel Memorial Lecture

## Changing Patterns of Disease*

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OF THE many unusual events which characterized the first half of the present century, especially in this country, one of particular significance to medicine was the development of marked changes in established patterns of disease. Tonight I wish to discuss a few of these changes from the standpoints of their nature and their underlying causes. The ones to be considered are the resultants of a series of medical discoveries which themselves were fitting accompaniments of a truly remarkable half-century. Over a period of but a few decades pathologic patterns originally established as a result of bacterial interactions with tissues merged into patterns of viral dominance and then into alterations produced by an increasing variety of metabolic, neoplastic, and retrogressive stimuli. In the course of these changes some of the older diseases tended to disappear, to be replaced by newer diseases and by newer problems. The disappearance of the older diseases is a fitting testimonial to the creative talents of the many gifted scientists who, through their discoveries, displayed some of the artistic and scholarly attributes which constitute the essential core of the humanities as we now conceive them.

### ADVANCES IN MEDICINE IN THE PAST HALF-CENTURY

At the beginning of the century the common pattern of disease was unquestionably the product mainly of bacterial action. In those days a large portion of a physician's time was taken up with the handling of tuberculosis, syphilis, typhoid fever, dysentery, scarlet fever, meningitis, erysipelas, whooping cough, diphtheria, pneumonia, tetanus, puerperal sepsis, ear infections, rheumatic disease, surgical infections, malaria, and even at times, smallpox. Unfortunately, the physician himself was ill-prepared to treat these diseases. In comparison with today's standards his medical training was lamentably brief and his diagnostic facilities were severely limited. The roentgen-ray machine was just coming into general use, laboratories were few, most of them were poorly manned, electrocardiography was in its early developmental stages, and knowledge of metabolic abnormalities was fragmentary. There was at best a very meager assortment of pharmaceutical products suitable for specific needs. General practice was the rule and the idea of Specialty Boards and their appropriate Colleges was yet unborn. Under these circumstances the family doctor too often had no choice but to dispense consolation in lieu of specific medication.

Even then, however, the expanding forces of preventive and curative medicine were coming into action. For example, the procedures of pasteurization of milk and purification of water were gaining momentum; the immunizing potentialities of diphtheria, tetanus, typhoid and pertussis bacilli were becoming manifest; and antibacterial chemotherapy was already more than a dream in the mind of Ehrlich. Nevertheless, not many persons foresaw at this time the approaching activation of the huge medical potential which was soon to be revealed in terms

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of so many unusually significant medical discoveries, including blood groups, toxoids, vitamins, synthetic amino acids, hormones, heparin and dicoumarol, DDT, sulfonamides, antibiotics, isotopes, newer anesthetic agents, and scores of useful drugs, among them the so-called antihistaminics, anticholinergics, antihypertensives, the tranquilizers, and now, even the anticholesterolics.

The impact of these developments upon different patterns of disease was soon evidenced in a variety of ways, viz., (1) in the virtual disappearance of most of the known deficiency diseases, such as pernicious anemia, pellagra, rickets, scurvy, beri beri, and, in some areas, nodular goiter; (2) in the prolongation of useful and happy lives for thousands of diabetic subjects; (3) in the unparalleled acceleration of surgical therapy through the development of blood banks, better nutritional and electrolyte management, and improved methods and types of anesthesia, thereby making possible the massive resections of cancer therapy and the complicated operations now customary in cardiovascular, thoracic and neural surgery; (4) in the almost total elimination of the terrors of diphtheria, tetanus, whooping cough and, now, of poliomyelitis; (5) in the near-elimination, through the use of DDT, of typhus, yellow fever and malaria; (6) in the amelioration of various kinds of hormonal deficiencies and in the treatment of certain types of cancer through the use of an increasing assortment of hormonal preparations.

## Effects of Control of Bacterial Infection on Cardiology

Of all the changes in disease patterns, however, the most spectacular were those stemming from the therapeutic actions of the sulfonamides and antibiotics. The effects of this breakthrough upon the total pattern of disease are even now not entirely comprehended. For instance, a recent estimate by Dauer of the United States Public Health Service suggests that in the first 15 years of the sulfonamide-antibiotic era about one and one-half million lives were saved in the United States alone. These represent individuals who probably would have died if the death rates for certain infectious diseases had followed the same trends after 1937 as they had before.

Because of these salvaged lives increasing numbers of survivors now present new varieties of disease patterns in relation to cardiovascular, neoplastic, arthritic or cerebral derangement. The pertinent question is: Will the therapeutic measures available now or later be as effective in the treatment of metabolic and degenerative maladies as was chemotherapy in relation to infection? The question is no less challenging to the cardiologist, for the changes in patterns of cardiovascular disease have certainly been as extensive as they have been in other fields of medicine. Accordingly, with the diminution of so many kinds of infectious disease the cardiologist can surely look forward to a time of fewer complications of heart disease. Thus when tuberculosis and syphilis have ceased to be major infective threats, when pneumococcic and streptococcic infections have become minor or even occasional causes of disease, a variety of infective sequelae, such as adhesive pericarditis, bacterial endocarditis, thoracic aortic aneurysm, myocarditis, and possibly nephritis and pyelonephritis, will surely lose a great deal of their cardiologic significance.

Perhaps by then the cardiologist also will have lost much of his interest in hemodynamics and, instead, will have become an expert in metabolism, attempting where Ponce de Leon failed, to extend the boundaries of life, not by the discovery of the fountain of youth, but by the administration of a low-fat, low-calorie, low-salt, low-cost diet to centenarians leading the stressless and alarmless life of suprarenal, pituitary and gonadal hypoplasia. Let us hope, however, that at the same time economic hard times, brought about by or accelerated by political action and civilian indifference, will not then have made the rice diet as common in this country as it is now in Asia. This would surely not be the happiest way to solve our current problems of atheromatosis, hypertension and obesity.

## Chemotherapy and the Changing Patterns of Infection

But let us reject such a gloomy outlook and look back instead to some recent happenings

relating to the two major infectious diseases of our time, *syphilis* and *tuberculosis*.

*Syphilis:* It is indeed startling to recall that only about two decades ago (in 1937) J. E. Moore, then editor of the *American Journal of Syphilis*, emphasized the two points which, in his opinion, made syphilis the greatest of modern public health problems. These were its prevalence and its appalling tendency to produce chronic invalidism or death. Seventeen years later, in 1954, this same editor announced the discontinuance of the *American Journal of Syphilis* because of a lack of manuscripts and of interest in the subject. Similarly in 1955 the chief editor of the *A.M.A. Archives of Dermatology and Syphilology* announced the deletion of the word Syphilology because of the decline in syphilis. In short, within a few years there had been a falling-off of approximately 75 to 90 per cent in the number of cases of fresh syphilitic infection reported throughout the entire continental United States. Concurrently the rates for lethal syphilitic lesions, as established by necropsy findings, had similarly declined.[1] Thus, after only a few years it had become apparent that penicillin possessed the capacity, when properly used, to eliminate one of mankind's greatest scourges.

*Tuberculosis:* In the same period comparable changes in mortality rates for tuberculosis had likewise occurred. These were evidenced by a steady fall in death rates for primary and reinfection types, for miliary tuberculosis and for tuberculous meningitis. Particularly impressive also was the decline in mortality for renal tuberculosis. It is not surprising, therefore, that recently so many tuberculosis sanitaria have shifted their attention to geriatrics.

Thus in approximately 20 years two of our most aggressive infectious diseases have been decisively reduced to the status of second-class microbic powers.

*Other Bacterial Infections:* A similar pattern has been observed, also, for other types of infection. A few years ago I pointed out some of the changing patterns of infection as disclosed by the findings in several thousand consecutive necropsies performed in the University of Chicago Clinics between the years 1927 and 1952.[2] The infections under scrutiny were lobar pneumonia, acute purulent meningitis, bacterial endocarditis, generalized peritonitis and acute perforative appendicitis. In a smaller series of necropsies performed in the Chicago Lying-In Hospital between the years 1927 and 1954 the changes with reference to serious obstetric and gynecologic infections were also reviewed.

On the basis of the incidence of types of infection in relation to each 500 necropsies it was evident that in all categories the death rates had fallen steadily. Thus, during the chemotherapeutic era lobar pneumonia and bacterial meningitis ceased to be important causes of death, puerperal sepsis practically disappeared, and the death curves for generalized peritonitis and perforative appendicitis steadily declined.

Corresponding trends have been seen, also, for other types of infection. Thus, acute hematogenous osteomyelitis and tuberculosis of the bones and joints have almost vanished from the orthopedic wards. With them have gone most instances of secondary amyloidosis, and today amyloid disease is seen mainly in its primary form. Even the diagnosis of primary cardiac amyloidosis is no longer a rare event.

*Contagious Diseases:* Of other contagious diseases, diphtheria, scarlet fever, and erysipelas also have become almost medical curiosities. In the Chicago Municipal Hospital Hoyne has reported that, whereas in 1928 admissions for diphtheria numbered 1,009, with a death rate of 16 per cent, in 1948 there were only eight admissions and there were no deaths.[3] In the same hospital in 1934 there were 3,000 admissions for scarlet fever, with 47 deaths; in 1948, however, there were only 249 admissions, with no deaths. With reference to erysipelas Hoyne reports that in the Cook County Contagious Disease Hospital during the years 1934 to 1938 inclusive, 998 patients were treated, with a fatality rate of 17.3 per cent. In contrast, during the years 1951 to 1955 inclusive, only 77 patients were treated and there was only one death.

Thus, in an amazingly short time chemotherapy has functioned effectively both to terminate developed infections and, more importantly, to prevent their further spread through the breaking of chains of contagion. In conse-

quence, but excluding the currently difficult problem of hospital infections by antibiotic-resistant staphylococci, there is now reason to believe that the incidence of nosocomial infection in hospitals is definitely below that of the preantibiotic era. Where the question has been specifically studied the decline has been coincident with the expanding use of sulfonamides and antibiotics. This suggests that in general the hospital environment today is less heavily contaminated by potentially pathogenic micro-organisms and that there are fewer dispersers of these bacteria among patients and personnel.

*Viral Diseases:* In view of the presumed environmental reduction in the pathogenic bacterial population it is not surprising that viral diseases, especially those affecting the respiratory tract, have come into greater prominence. This changing pattern of infection may be attributed to the growing interest in viruses and in the diagnosis of viral diseases as well as to the probability that viruses can now manifest their pathogenic potentialities without the effects being obscured by concomitant bacterial growth. Fortunately, most of the viral diseases are more disabling than lethal, especially the commonest ones such as measles, mumps, rubella, chickenpox, influenza, poliomyelitis, encephalitis, infectious hepatitis, atypical pneumonia, the common cold, and the adenovirus infections.

## Disease Patterns Resulting from Drug Therapy

Thus far we have been concerned mainly with patterns of disease which are the products of an interaction between drugs and bacteria or viruses within the tissues. Let us now examine a pattern of disease which results from the actions of drugs upon the tissues themselves. In other words disease patterns, the result of therapy, constitute a type of pathologic change which needs to be more clearly understood if we are to avoid the paradoxic situation in which the cure sometimes becomes worse than the disease. A case in point is that of the Elixir of Sulfanilamide episode in which over 80 persons died of renal failure from the taking of sulfanilamide dissolved in diethylene glycol. The fact that the employee of the drug firm responsible for the error committed suicide did not atone for the initial failure to ascertain that the solvent was deleterious to tissues.

Those who ponder the problem of iatrogenic disease as we see it today are often inclined to justify much of it on the ground that we perforce must pay a certain price for progress. An essential part of this price is the taking of a calculated risk. Certainly the concept is not new in medical thought; as long ago as the 18th century variolation for the prevention of smallpox was practiced widely despite the lethal risk. Similar hazards were faced more recently in the testing of the vaccine against poliomyelitis; and risks are taken daily by physicians everywhere in their decisions regarding therapy, especially surgical. The greatest difficulty about the calculated risk, however, will always be this: How sure can one be of the wisdom and mathematical competence of the calculator?

*Myelotoxic Reactions:* The seriousness of the problem is compounded by the fact that new drugs are appearing faster than the safety of the older ones can be adequately assured. It is not surprising, therefore, that myelotoxic reactions once considered unusual are now pathologic commonplaces. These include granulocytopenia, thrombocytopenia, aplastic anemia, as well as acute anaphylactic reactions, urticaria, angioneurotic edema, arteritis, myocarditis, neuritis, etc. In the case of some of the antileukemic agents used with antibiotics because of a developing granulocytopenia, transformation of the intestinal flora to a monilial or micrococcic type leads at times to further complications such as enterocolitis or blood stream invasion. With the mounting use of adrenal steroids complications ranging from activation of tuberculosis, perforation of peptic ulcer and development of spontaneous peritonitis to extreme osteoporosis and pathologic fracture have been seen. Even the tranquilizers have presented unforeseen difficulties when used in excessive amounts.

*Carcinogenic Reactions:* In many of these situations there is fairly general agreement that the taking of therapeutic risks is justified because of the desperate nature of the disease itself. The calculated risk becomes less justi-

fied, however, when therapeutic agents of unknown nature are employed, and all the more so when the agents have carcinogenic potentialities.

For example, a few decades ago there was a vogue for the use of radium water in the treatment of arthritis and of radium chloride in schizophrenia. Those who prescribed these materials were of course not aware of the long induction times often associated with carcinogenesis nor of the carcinogenic potentialities of ionizing radiation. Years later radiation necrosis of bone and osteogenic sarcoma have developed in some of these patients. Likewise cases of reticulum cell sarcoma have appeared years after intravenous injections of thorotrast for diagnostic purposes. Even today we are ignorant of the possible leukemogenic properties of some of the radioactive isotopes and we are also uncertain concerning the wisdom of using x-ray therapy in children for certain benign lesions of the upper thorax because of the possibility of later development of cancer of the thyroid gland or even of leukemia. Somewhat unsettling also is the experimental evidence that Evans blue, congo red, and PVP are carcinogenic for some of the lower animals.

These instances of iatrogenic disease at least raise the question whether it is justifiable to treat a disease of unknown nature with a drug of unknown action. They also emphasize the need for continuous scrutiny of all changing patterns of disease by necropsies in order to keep continually alerted to the possibilities of unanticipated dangers.

## Effect of Changes in Environment

The changes thus far considered seem of almost minor pathologic significance in comparison with those resulting from the exposure of whole populations to ionizing radiation. Certainly the increase in leukemia among the citizens at Hiroshima and Nagasaki and the current problems of radioactive fallout are opening up new possibilities of changing patterns of disease, patterns which may manifest themselves as bone marrow injury, neoplastic change, or through their genetic effects. Because of these possibilities, however, these questions are no longer solely matters of medical concern but encompass questions of scientific, military, and political judgment.

But even before the advent of the Atomic Age the problems of industrial disease were becoming increasingly urgent; and with them came the assumption that increasing complexities of living would produce new forms of disease. Hence we hear a great deal nowadays about stress diseases, alarm reactions, diseases of adaptation, about "worry nerves," hazards of smoke and smog, of chemical additives in our food, etc. Obviously most of these questions are still in their conjectural phases; what we particularly need to know is: Can we be sure that there has been an actual increase in mental disease, in coronary thrombosis, in hypertension, in cancer, etc? It is unfortunate that, because our base-line data are so inadequate, it is impossible to know for certain whether these changing patterns are new or are merely newly found. Moreover, we have little reason to hope that these problems can be solved by the perusal of death certificates; and it will be many years before necropsy percentages attain a level for the country as a whole adequate to provide answers to many of these questions.

Our changing environment unquestionably has led to concomitant changes in patterns of disease. This has been particularly true in the field of cancer, because of exposures of many persons to increasing numbers of carcinogenic agents, because of an ever-greater production of chemical compounds of carcinogenic potentiality, and because of an aging population. Due to the current interest in the question of cancer of the lung more attention is now being paid to the problem of air pollution by potential carcinogens. This represents a striking shift in interest with reference to air-borne disease inasmuch as only recently our principal concern centered around the relationship of bacterial dissemination to respiratory disease.

*Air-Pollution and Cancer:* Although information concerning air pollution by toxic agents is still relatively meager, pertinent data are accumulating. Thus workers in England have reported that concentrations of smoke, sulfur dioxide, benzpyrene, and other polycyclic hydrocarbons rise with increasing urbanization; and in Liverpool they have found amounts of

benzpyrene in the air from eight to eleven times those of rural air. Elsewhere the concentrations of benzpyrene in smog-filled air have been found to be about four times those of normal air; and studies on the carcinogen content of gasoline engine exhausts have revealed the presence of considerable amounts of benzpyrene, particularly when the motor was idling.

In short, in our industrial cities there is evidence that we are living more or less continuously in a "carcinogenic sea" made turbid by industrial wastes of various sorts. In such an environment it is impossible to avoid daily contacts with carcinogens of different kinds which may be present in smoke, in auto and diesel fumes, in dusts from tarred, oiled or asphalted roads, in carbon blacks from tire friction, and, at times, in association with asbestos, chromates, arsenic, nickel, beryllium, oil refinery products, isopropyl oils, radioactive materials, etc. One may justifiably wonder, therefore, about the association of such conditions with the fact that in 50 years cancer has risen as a cause of death from eighth to second place. I might add that in a recent series of 1,000 consecutive necropsies from our files, 560 showed malignancy.

*Cancer of the Lung:* Perhaps cancer of the lung may serve as a prototype for some of the changing patterns of disease which are the resultants of changing environmental factors. It now seems to be generally agreed that the increase in this type of cancer is real and that it is most probably caused by some sort of environmental stimulus. The most controversial aspect of the question still pertains to the possible role of inhaled smoke, whether from cigarettes or from industrial or automotive sources. Assuming for the moment, therefore, that the inhalation of smoke or fumes is an important pathogenetic factor, it is interesting to reflect that the cigarette manufacturers have gone to a great deal of trouble to provide filter tips and milder forms of tobacco whereas, in contrast, few of us have expressed any concern whatever about the possible hazards related to the inhalation of fumes from automobiles and diesel motors lined up at red lights as their idling motors spew out unknown quantities of benzpyrene and other hydrocarbons. In fact for most of us the red lights are merely traffic restrictions rather than reminders of possible cancer dangers.

## Conclusion

In closing I would like to re-emphasize the point that I have tried to consider only patterns of disease which have resulted from newer kinds of stimuli. These stimuli represent either newer forms of therapy or altered conditions of living. On the other hand, I have omitted reference to diseases which are only newly revealed rather than newly created. For example, it was the large-scale development of blood banks which led to the increased frequency of homologous serum jaundice, of renal failure and of Rh incompatibilities; it was the wide-spread use of medicated mineral oil which led to lipid pneumonia; it was excessive radiation over the abdomen which led to radiation nephritis and its associated hypertension; and it was the immoderate administration of oxygen to premature infants which eventuated in retrolental fibroplasia.

If from the experiences of the past 50 years we have learned in some measure to foretell events to come in the next 50 years, we can surely expect to see continuing changes in patterns of disease. Certainly it is not difficult to believe that more of the viral diseases will tend to disappear as suitable vaccines become available. It is also not difficult to believe that as the causes underlying the development of degenerative and neoplastic diseases become more evident, preventive and curative measures will emerge to eliminate them. The biggest obstacle to the ultimate control of many diseases will probably continue to be the inability of man himself to counteract his tendency to collective self-destruction as, for example, by hydrogen bombs and intercontinental missiles. But unless he can control these agents there will be little reason for optimism in relation to his present-day vigorous attacks on metabolic disease. It is inconceivable, however, that the unparalleled achievements of the first half of the 20th century will be nullified by the destructive release of nuclear energy in the second half.

There is an old story about a medieval alchemist who, as his life was drawing to a close, succeeded finally in discovering the magic drug

which, in his opinion, possessed the capability of curing every human malady. Unfortunately, when he approached his terminal illness and confidently imbibed a generous portion of this precious remedy, he found to his consternation that it had one serious limitation; it was able to cure every malady except the final one.

Our modern alchemist has gone much farther than did his medieval brother. Although he too has not found it feasible to transmute base metals into gold, his radioactive isotopes are transforming or establishing disease patterns in a variety of ways. On the one hand the isotopes of iodine and phosphorus are performing effectively in the therapy of certain diseases of the thyroid gland or bone marrow. On the other hand, strontium 90 is presenting an increasing menace in its relationship to fallout. Thus mankind again faces the age-old problem of the choice between good and evil. But the big problem posed by the modern alchemist is: Will this choice be the final one?

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# Seminar on Ballistocardiography

*Guest Editor*

SIDNEY R. ARBEIT


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# The Nature of Records from Ultra-Low Frequency Ballistocardiographic Systems and Their Relation to Circulatory Events*

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## INTRODUCTION

ALTHOUGH the two earliest investigators (Gordon[1] in 1877 and Henderson[2] in 1905) in the field now known as ballistocardiography used pendular "beds" very loosely coupled to earth and with low natural frequency, most of the work in this research area has been carried out with systems having stiffer couplings and higher natural frequencies. The origin of ballistocardiography as a definite discipline dates back only to 1939 when Starr[3] developed a rugged practical "high-frequency" bed which could be applied on a relatively broad scale to the study of clinical and physiologic problems in patients. His pioneering work with this instrument was directly responsible for the rapid and continued growth of the field.

The recent revival of interest in the earlier methods has stemmed, in large measure, from biophysical studies conducted by Burger,[4] von Wittern[5] and Talbot,[6] the results of which were in rather close agreement. These investigators concluded that when the body's support is heavy and/or stiffly coupled to earth, records of body motion so obtained are very seriously distorted, but that these errors could be minimized by using a light support with a very soft coupling to earth. These requirements have been realized in several ways and a number of different designs have been recently devised and put into use[4,5,7–10] They have in common a lightweight supporting surface and a low natural frequency (0.5 c/s or less). They appear to yield comparable records and have been designated "ultra-low frequency ballistocardiographs"[11] to distinguish them from the beds of the Nickerson type with different characteristics (heavier platform, greater damping and higher frequency). The design of the latter was chosen for practical reasons, although Nickerson[12] clearly demonstrated the desirability of using a suspension with a natural frequency less than 1 c/s.

The early records obtained by both Gordon and Henderson were of the displacement type only, since suitable velocity and acceleration transducers have been a relatively recent development. The newer ultra-low frequency systems have had but limited clinical trial thus far. Most of the experience has been gained with acceleration records and information regarding displacement and velocity records has been meager. A notable exception is the excellent work carried out in Holland by Elsbach[13] using a bed based on the Burger design. His is the only sizable clinical study which has

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The views expressed herein represent those of a group which includes, in addition to the authors, Drs. S. A. Talbot, Benjamin M. Baker, Jr., F. W. Davis, Jr., M. L. Singewald and R. E. Mason.

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yet appeared. Unfortunately, his results were in the form of a monograph in Dutch which made them rather inaccessible to most investigators in this country.* His clinical material included groups of normal subjects and patients with various types of cardiovascular disease. Various time and amplitude measurements were made on the head-foot displacement, velocity, and acceleration records obtained from the normal subjects. However, since his instrument had no amplitude calibration, there were no absolute amplitude measurements.

The importance of recording displacement, velocity and acceleration records lies in the fact that they contain information of a different though complementary sort about dynamic circulatory behavior. When the human body is suspended or "floated" in such a way that it is free of frictional and restoring forces, then a change in the center of gravity of the blood's mass within the body will cause the rest of the body and its support to move in the opposite direction so that the center of gravity of the system as a whole will remain unchanged. The mass movements of the body will be equal to the mass movements of the blood but opposite in direction. The mass-displacement of the body (the product of the externally observed displacement of the body and the mass of body and support) will equal the internal mass-displacement of blood (mass of blood $\times$ its displacement). Similarly, the momentum (mass $\times$ velocity) of body and blood can be equated, as can force (mass $\times$ acceleration) of body and blood.

Ultra-low frequency ballistocardiographs of various types have been under investigation in this laboratory for several years. The purpose of this report will be to describe a type of instrument which has proven practical and convenient, and to consider the nature of the records (displacement, velocity, and acceleration) obtained with it and their relation to circulatory events.

Detailed time and amplitude measurements have been made on the simultaneously recorded head-foot displacement, velocity, and acceleration ballistocardiograms from 100 normal subjects less than 40 years of age. Some of the results are to be reported here while the remainder will be the subject of a subsequent publication.

* An English translation of Elsbach's monograph has recently been re-edited by one of us (W. R. S.) and a limited number of copies are available for distribution.

## Methods

### Recording procedures

The ultra-low frequency ballistocardiograph, transducers and associated electronic equipment used in these studies are described in detail in the appendix.

A standard laboratory test procedure has been carried out on sizable groups of normal subjects and patients with various types of cardiovascular disease. No attempt was made to conduct these studies under basal conditions.

After the subject reclined on the ballistocardiograph with a small pillow or pad beneath the head, chest constraint blocks were applied and the footboard adjusted to the proper position with the knees slightly flexed; when the legs were straightened, the dorsal tissues were placed under stress thus improving the coupling between the body and the platform. Electrocardiographic electrodes were strapped on, a crystal microphone (Cambridge) was positioned over the cardiac apex for heart sounds and a pneumo belt (strain gauge) placed for recording respiratory chest movements. The subject was then allowed to rest quietly for 10 to 15 minutes.

*During normal breathing* the following tracings were recorded simultaneously on a 6-channel Hathaway oscillographic recorder: head-foot acceleration BCG (HF-A), lateral acceleration BCG (Lat-A), pneumogram, electrocardiogram (lead II), and phonocardiogram (apex).

*During suspended respiration* the following tracings were recorded simultaneously: head-foot displacement (HF-D), velocity (HF-V) and acceleration (HF-A) ballistocardiograms, lateral acceleration ballistocardiogram, electrocardiogram and phonocardiogram. At least one record was obtained with respiration suspended at each of three respiratory positions: mid-inspiration, the end of normal inspiration, and the end of normal expiration. The subjects were given careful instructions about suspending respiration and were urged to try to remain as relaxed and motionless as possible. Such precautions are necessary if reasonably stable displacement and velocity records are to be obtained. In some subjects additional tracings

were obtained during suspended respiration with the lateral displacement ballistocardiogram (photoelectric transducer) or the carotid pulse (crystal or condenser pickups) being recorded instead of the head-foot velocity ballistocardiogram.

These records were obtained on 6 inch photographic paper at a speed of 5.0 cm/sec. In each subject a calibration record was obtained of the electrical gain of the amplifiers used for the three head-foot ballistocardiograms and the lateral acceleration ballistocardiogram.

### ANALYSIS OF THE RECORDS FROM YOUNG NORMAL SUBJECTS

Detailed time and amplitude measurements were carried out on the records from 100 normal subjects less than 40 years of age. There were 25 subjects in each of four age groups: males 20 to 29 yrs, males 30 to 39, females 20 to 29 and females 30 to 39 years of age. These groups were made up of student and graduate nurses, medical students, staff physicians, secretaries, technicians, and other hospital personnel. They were all healthy and active and were judged to be normal on the basis of the following criteria: (1) no symptoms or history of heart disease; (2) heart normal in size and shape roentgenographically; (3) absence of cardiac murmurs; (4) normal 12-lead electrocardiogram; (5) blood pressure within normal limits (less than 140/90).

Although more extensive measurements were made, only the more important ones from the head-foot displacement, velocity, and acceleration ballistocardiograms are included here.

#### (*1*) *Baselines*

(*a*) *Acceleration Ballistocardiograms:* In the records during suspended and normal respiration, a horizontal baseline was drawn through the relatively steady and straight diastolic portions of successive complexes. In a few cases during normal breathing there was too much slow respiratory weave to allow a single baseline to be drawn through all complexes in a respiratory cycle; in such cases a correction was made by replacing the baseline.

(*b*) *Displacement Ballistocardiograms:* Since there is no true baseline for these records, the selection of a baseline is arbitrary. In each complex to be measured a horizontal line was drawn through it at the level of the I maximum.

(*c*) *Velocity Ballistocardiograms:* The the baseline chosen here was that of zero velocity. Multiple points in a number of velocity complexes were selected by reference to synchronous points in the simultaneous displacement record and a horizontal baseline drawn through them. Zero velocity was most reliably established if in the displacement record there were two or more sections (usually in diastole) which were straight, horizontal and of reasonable length (0.1 sec or more). If such flat portions of the displacement curve could not be found, zero velocity was taken as the point at which the displacement curve showed complete reversal in direction (for example, at the tips of J and M) for at such curvatures velocity passes through zero.*

#### (*2*) *Time Measurements*

Time measurements were made only from the records obtained during suspended respiration. In some 30 or 40 subjects all time intervals were measured in the records from all three respiratory positions (mid-inspiration, end-inspiration, and end-expiration). Inasmuch as there appeared to be no consistent differences in the values from the three records they were averaged. In the rest of the subjects measurements were taken from only one record (usually mid-inspiration) or from two (usually end-inspiration and end-expiration) and averaged.

In each record one or two cardiac cycles in which the BCG complexes were consistent and typical were chosen for measurement. The onset of the Q wave of the electrocardiogram served as the time reference and all measurements made from it; events preceding the Q wave were given negative signs, those following it positive signs. Measurements were made to the nearest 0.005 sec. For heart sounds time was measured from the Q wave to the onset of the initial rapid vibration of the 1st and 2nd sounds and, when present, to the onsets of the 3rd sound ($S_3$) and the atrial sound ($S_a$). The BCG time intervals measured are shown in Tables I, II, and III. Figure 1 illustrates the method used for designating waves in the three head-foot ballistocardiograms; this conforms to that proposed by the American Heart Association Committee on Ballistocardiographic Terminology,[11] but a few additional symbols

* The baseline could also be determined by planimetry or by quickly reducing the electrical amplification, provided this latter does not alter the position of the tracing on the paper.

## TABLE I
### Time Measurements

| | | Electrocardiogram and heart sounds | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | R-R | Heart rate | P-R | P-$S_a$ | Q-$S_a$ | Q-$S_1$ | Q-$S_2$ | Q-$S_3$ |
| **Males** | | | | | | | | | |
| 20–29 yr | number | 25 | 25 | 25 | 9 | 7 | 24 | 24 | 17 |
| | Mean | 0.9814 | 62.184 | 0.1578 | 0.1277 | −0.0397 | 0.0626 | 0.3970 | 0.5379 |
| | S.D. | 0.1220 | 8.45 | 0.0176 | 0.0241 | 0.0186 | 0.0095 | 0.0218 | 0.0358 |
| 30–39 yr | number | 25 | 25 | 25 | 10 | 10 | 25 | 25 | 12 |
| | Mean | 0.9149 | 66.652 | 0.1618 | 0.1130 | −0.0560 | 0.0568 | 0.3824 | 0.5250 |
| | S.D. | 0.1175 | 8.28 | 0.0185 | 0.0149 | 0.0156 | 0.0096 | 0.0188 | 0.0121 |
| Difference (d) in means* | | +0.06652 | −4.468 | −0.0040 | +0.0147 | −0.0163 | +0.0058 | +0.0146 | +0.0129 |
| | d/S.E. | 1.96 | 1.89 | 0.78 | 1.58 | 1.91 | 2.12 | 2.58 | 0.90 |
| **Females** | | | | | | | | | |
| 20–29 yr | number | 25 | 25 | 25 | 11 | 11 | 25 | 25 | 18 |
| | Mean | 0.8880 | 69.340 | 0.1490 | 0.0991 | −0.0496 | 0.0559 | 0.3942 | 0.5356 |
| | S.D. | 0.1460 | 10.87 | 0.0143 | 0.0133 | 0.0105 | 0.0097 | 0.0254 | 0.0124 |
| 30–39 yr | number | 25 | 25 | 25 | 9 | 9 | 25 | 25 | 9 |
| | Mean | 0.8363 | 72.504 | 0.1518 | 0.1172 | −0.0467 | 0.0550 | 0.3888 | 0.5256 |
| | S.D. | 0.0904 | 7.38 | 0.0189 | 0.0246 | 0.0170 | 0.0065 | 0.0185 | 0.0198 |
| Difference (d) in means* | | +0.05168 | −3.164 | −0.0028 | −0.0181 | +0.0029 | +0.0009 | +0.0054 | +0.0099 |
| | d/S.E. | 1.51 | 1.20 | 0.59 | 1.98 | 0.60 | 0.39 | 0.85 | 0.88 |
| **Males** | | | | | | | | | |
| 20–39 yr | n | 50 | 50 | 50 | 19 | 17 | 49 | 49 | 29 |
| | Mean | 0.9482 | 64.418 | 0.1598 | 0.1200 | −0.0493 | 0.0597 | 0.3896 | 0.5326 |
| | S.D. | 0.124 | 8.55 | 0.0179 | 0.0211 | 0.0187 | 0.0100 | 0.0211 | 0.0374 |
| | ±2 S.D. | 0.700 to | 47.08 to | 0.124 to | 0.078 to | −0.012 to | 0.040 to | 0.347 to | 0.458 to |
| | range | 1.196 | 81.28 | 0.196 | 0.162 | −0.087 | 0.080 | 0.432 | 0.607 |
| **Females** | | | | | | | | | |
| 20–39 yr | number | 50 | 50 | 50 | 20 | 20 | 50 | 50 | 27 |
| | Mean | 0.8622 | 70.922 | 0.1504 | 0.1073 | −0.0483 | 0.0555 | 0.3915 | 0.5322 |
| | S.D. | 0.1240 | 9.42 | 0.0168 | 0.0212 | 0.0139 | 0.0083 | 0.0223 | 0.0343 |
| | ±2 S.D. | 0.614 to | 52.08 to | 0.117 to | 0.065 to | −0.021 to | 0.040 to | 0.347 to | 0.464 to |
| | range | 1.110 | 89.76 | 0.184 | 0.150 | −0.076 | 0.072 | 0.436 | 0.601 |
| Difference (d) in means* | | +0.08602 | −6.5040 | +0.00938 | +0.01275 | +0.00104 | +0.00419 | −0.00193 | +0.00036 |
| | d/S.E. | 3.47 | 3.59 | 2.71 | 1.88 | 0.19 | 2.23 | 0.44 | 0.04 |

* For all differences in means, the 4th decade mean is subtracted from the 3rd. Therefore, if the difference is preceded by a positive sign, the 3rd decade mean is the larger; if preceded by a negative sign, it is the smaller. This convention is used in all tables.

TABLE II

Time Measurements

| | | Displacement ballistocardiogram | | | | | Velocity ballistocardiogram | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Q-″$G_0$ | Q-″H | Q-″I | Q-″J | Q-′M | Q-′H | Q-′I | Q-′J | Q-′L | Q-′M | $'I_t$ | $'J_t$ |
| **Males** | | | | | | | | | | | | | |
| 20–29 yr | n | 15 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 24 | 25 | 25 |
| | Mean | −0.0612 | 0.0889 | 0.1371 | 0.2359 | 0.4504 | 0.1182 | 0.1868 | 0.3138 | 0.4318 | 0.5170 | 0.1000 | 0.2224 |
| | S.D. | 0.0144 | 0.0244 | 0.0107 | 0.0175 | 0.0193 | 0.0120 | 0.0114 | 0.0168 | 0.0208 | 0.0265 | 0.0149 | 0.0215 |
| 30–39 yr | n | 17 | 24 | 25 | 25 | 25 | 25 | 25 | 25 | 24 | 20 | 25 | 25 |
| | Mean | −0.0665 | 0.0850 | 0.1317 | 0.2196 | 0.4286 | 0.1118 | 0.1765 | 0.2954 | 0.4203 | 0.5033 | 0.0949 | 0.2084 |
| | S.D. | 0.0200 | 0.0214 | 0.0145 | 0.0194 | 0.0261 | 0.0132 | 0.0164 | 0.0212 | 0.0203 | 0.0300 | 0.0221 | 0.0340 |
| Difference (d) | in means | −0.0053 | +0.0039 | +0.0054 | +0.0163 | +0.0218 | +0.0064 | +0.0102 | +0.0184 | +0.0115 | +0.0138 | +0.0051 | +0.0140 |
| | d/S.E. | 0.87 | 0.60 | 1.50 | 3.13 | 3.37 | 1.80 | 2.56 | 3.42 | 1.50 | 1.62 | 0.96 | 1.75 |
| **Females** | | | | | | | | | | | | | |
| 20–29 yr | n | 12 | 23 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| | Mean | −0.0767 | 0.0870 | 0.1264 | 0.2172 | 0.4413 | 0.1079 | 0.1700 | 0.2900 | 0.4251 | 0.4955 | 0.0936 | 0.2305 |
| | S.D. | 0.0210 | 0.0157 | 0.0144 | 0.0153 | 0.0258 | 0.0136 | 0.0131 | 0.0268 | 0.0244 | 0.0303 | 0.0151 | 0.0197 |
| 30–39 yr | n | 13 | 23 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| | Mean | −0.0815 | 0.0850 | 0.1296 | 0.2058 | 0.4236 | 0.1108 | 0.1689 | 0.2735 | 0.4196 | 0.4838 | 0.0790 | 0.2274 |
| | S.D. | 0.0263 | 0.0166 | 0.0097 | 0.0139 | 0.0295 | 0.0115 | 0.0099 | 0.0214 | 0.0170 | 0.0234 | 0.0119 | 0.0193 |
| Difference (d) | in means | −0.0049 | +0.0020 | −0.0032 | +0.0115 | +0.0177 | −0.0028 | +0.0011 | +0.0165 | +0.0055 | +0.0117 | +0.0146 | +0.0031 |
| | d/S.E. | 0.51 | 0.42 | 0.92 | 2.78 | 2.24 | 0.80 | 0.34 | 2.41 | 0.92 | 1.53 | 3.36 | 0.56 |
| **Males** | | | | | | | | | | | | | |
| 20–39 yr | n | 32 | 49 | 50 | 50 | 50 | 50 | 50 | 50 | 49 | 44 | 50 | 50 |
| | Mean | −0.0640 | 0.0870 | 0.1344 | 0.2278 | 0.4395 | 0.1150 | 0.1816 | 0.3046 | 0.4262 | 0.1508 | 0.0975 | 0.2154 |
| | S.D. | 0.0178 | 0.0220 | 0.0130 | 0.0200 | 0.0254 | 0.0130 | 0.0151 | 0.0213 | 0.0212 | 0.0289 | 0.0190 | 0.0292 |
| | ±2 S.D. range | −0.028− −0.100 | 0.043− 0.131 | 0.108− 0.160 | 0.188− 0.268 | 0.389− 0.490 | 0.089− 0.141 | 0.151− 0.212 | 0.262− 0.347 | 0.384− 0.469 | 0.453− 0.569 | 0.060− 0.136 | 0.157− 0.274 |
| **Females** | | | | | | | | | | | | | |
| 20–39 yr | n | 25 | 46 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| | Mean | 0.0792 | 0.0860 | 0.1280 | 0.2115 | 0.4325 | 0.1093 | 0.1697 | 0.2818 | 0.4223 | 0.4897 | 0.0863 | 0.2289 |
| | S.D. | 0.0240 | 0.0162 | 0.0124 | 0.0157 | 0.0294 | 0.0127 | 0.0082 | 0.0256 | 0.0212 | 0.0277 | 0.0170 | 0.0196 |
| | ±2 S.D. range | 0.031 to 0.127 | 0.054 to 0.118 | 0.103 to 0.153 | 0.180 to 0.243 | 0.374 to 0.491 | 0.084 to 0.135 | 0.153 to 0.186 | 0.231 to 0.330 | 0.380 to 0.465 | 0.434 to 0.545 | 0.052 to 0.120 | 0.190 to 0.268 |
| Difference (d) | in means | −0.0152 | +0.0010 | +0.00646 | +0.01628 | +0.0070 | +0.0057 | +0.01195 | +0.02286 | +0.00384 | +0.02111 | +0.01112 | −0.01352 |
| | d/S.E. | 2.67 | 0.25 | 2.54 | 4.52 | 1.29 | 2.22 | 4.93 | 4.87 | 0.90 | 3.60 | 3.09 | 3.54 |

## TABLE III

### Time Measurements

| | | Acceleration ballistocardiogram | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Q-$F_2$ | Q-$H_0$ | Q-H | Q-I | Q-J | Q-$L_0$ | Q-L | Q-M | Q-N | $I_t$ | $J_t$ |
| Males | | | | | | | | | | | | |
| 20–29 yr | n | 20 | 23 | 25 | 25 | 25 | 25 | 25 | 25 | 24 | 25 | 25 |
| | Mean | +0.0444 | 0.0688 | 0.1030 | 0.1564 | 0.2416 | 0.3979 | 0.4241 | 0.4575 | 0.5635 | 0.0676 | 0.1274 |
| | S.D. | 0.0200 | 0.0160 | 0.0125 | 0.0140 | 0.0164 | 0.0183 | 0.0204 | 0.0248 | 0.0335 | 0.0119 | 0.0096 |
| 30–39 yr | n | 21 | 24 | 25 | 25 | 25 | 25 | 25 | 25 | 24 | 25 | 25 |
| | Mean | +0.0516 | 0.0641 | 0.0983 | 0.1510 | 0.2280 | 0.3830 | 0.4128 | 0.4436 | 0.5494 | 0.0606 | 0.1257 |
| | S.D. | 0.0242 | 0.0222 | — | 0.0129 | 0.0212 | 0.0210 | 0.0218 | 0.0211 | 0.0255 | 0.0112 | 0.0131 |
| Difference (d) in means | | −0.0072 | +0.0047 | +0.0047 | +0.0054 | +0.0136 | +0.0149 | +0.0113 | +0.0139 | +0.0141 | +0.0070 | +0.0017 |
| | d/S.E. | 1.04 | 0.86 | 1.20 | 1.42 | 2.54 | 2.68 | 1.89 | 2.14 | 1.64 | 2.15 | 0.53 |
| Females | | | | | | | | | | | | |
| 20–29 yr | n | 16 | 25 | 20 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| | Mean | +0.0552 | 0.0702 | 0.0983 | 0.1488 | 0.2248 | 0.3898 | 0.4183 | 0.4507 | 0.5410 | 0.0600 | 0.1203 |
| | S.D. | 0.0160 | 0.0162 | 0.0144 | 0.0149 | 0.0156 | 0.0270 | 0.0247 | 0.0289 | 0.0361 | 0.0111 | 0.0134 |
| 30–39 yr | n | 21 | 21 | 25 | 25 | 25 | 25 | 25 | 25 | 23 | 25 | 25 |
| | Mean | +0.0485 | 0.0734 | 0.0999 | 0.1506 | 0.2077 | 0.3846 | 0.4117 | 0.4430 | 0.5470 | 0.0548 | 0.1122 |
| | S.D. | 0.0154 | 0.0139 | 0.0115 | 0.0079 | 0.0144 | 0.0182 | 0.0162 | 0.0179 | 0.0262 | 0.0104 | 0.0172 |
| Difference (d) in means | | +0.0067 | −0.0031 | −0.0016 | −0.0018 | +0.0171 | +0.0052 | +0.0066 | +0.0078 | −0.0060 | +0.0052 | +0.0081 |
| | d/S.E. | 1.28 | 0.66 | 0.43 | 0.53 | 4.04 | 0.80 | 1.11 | 1.14 | 0.66 | 1.72 | 1.85 |
| Males | | | | | | | | | | | | |
| 20–39 yr | n | 41 | 47 | 50 | 50 | 50 | 50 | 50 | 50 | 48 | 50 | 50 |
| | Mean | +0.0480 | 0.0064 | 0.1007 | 0.1537 | 0.2348 | 0.3904 | 0.4184 | 0.4506 | 0.5565 | 0.0641 | 0.1266 |
| | S.D. | 0.0223 | 0.0190 | 0.0141 | 0.0137 | 0.0203 | 0.0210 | 0.0226 | 0.0240 | 0.0306 | 0.0120 | 0.0114 |
| | ±2 S.D. | 0.003− | 0.028− | 0.073− | 0.126− | 0.194− | 0.348− | 0.373− | 0.403− | 0.495− | 0.040− | 0.104− |
| | range | 0.093 | 0.104 | 0.129 | 0.181 | 0.275 | 0.432 | 0.464 | 0.499 | 0.618 | 0.088 | 0.149 |
| Females | | | | | | | | | | | | |
| 20–39 yr | n | 37 | 41 | 50 | 50 | 50 | 50 | 50 | 50 | 48 | 50 | 50 |
| | Mean | +0.0514 | 0.0719 | 0.0991 | 0.1497 | 0.2162 | 0.3872 | 0.4150 | 0.4468 | 0.5439 | 0.0574 | 0.1163 |
| | S.D. | 0.0160 | 0.0151 | 0.0130 | 0.0119 | 0.0173 | 0.0232 | 0.0212 | 0.0243 | 0.0318 | 0.0111 | 0.0159 |
| | ±2 S.D. | 0.019− | 0.042− | 0.073− | 0.126− | 0.182− | 0.341− | 0.373− | 0.398− | 0.480− | 0.035− | 0.085− |
| | range | 0.083 | 0.102 | 0.125 | 0.174 | 0.251 | 0.434 | 0.457 | 0.495 | 0.608 | 0.080 | 0.148 |
| Difference (d) in means | | −0.00336 | −0.00547 | +0.00158 | +0.00400 | +0.01860 | +0.00326 | +0.00340 | +0.00374 | +0.01261 | +0.00672 | +0.01030 |
| | d/S.E. | 0.78 | 1.50 | 0.58 | 1.56 | 4.93 | 0.74 | 0.78 | 0.78 | 1.98 | 2.89 | 3.72 |

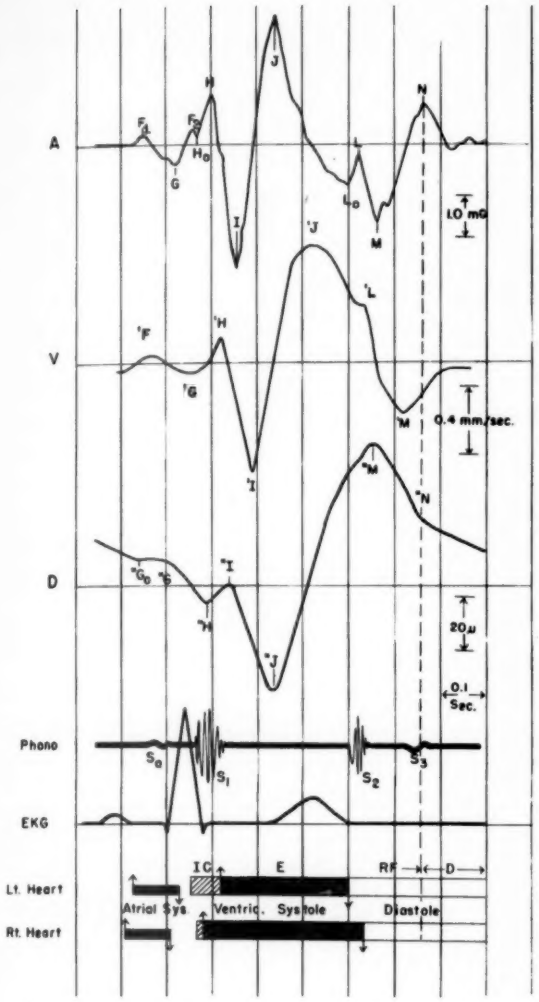


Fig. 1. Normal human displacement (D), velocity (V) and acceleration (A) ballistocardiograms from an ultra-low frequency (ULF) system and their temporal relation to events in the cardiac cycle. The BCG, heart sounds (phono), and ECG tracings were based on the measurements from 25 males, 20–29 years of age. The block diagrams at the bottom represent the timing of cardiac events on the two sides of the heart and are based on data supplied by Braunwald and by Wiggers (see text). IC = isometric contraction (crossed-hatched), E = ejection phase (solid black), RF = rapid filling, and D = diastasis.

Calibrations for the three ballistocardiograms are shown on the right. mG represents milli-G; 1.0 mG (0.001G) is approximately equal to 1.0 cm/sec²; $\mu$ represents micron; 20 $\mu$ is equal to 0.02 mm. The BCG tracings represent external motions of the body; headward motions are upwards. The tips of displacement waves should coincide in time with the tips of corresponding acceleration waves; however, the displacement waves are slightly advanced in time owing to the presence of a small phase lead.

were used. The subscript "o" was used after a few of the letters to indicate the onset of that particular wave or flexure. In displacement records $''G_o$ represents the onset of the ''G wave. See Figure 1 for the identity of the points $F_2$, $H_o$, and $L_o$. $F_2$ (positive) and $H_o$ (negative) are a pair of waves which precede the H wave and usually fall about the time of the onset of the 1st heart sound; they are rather variable and may be represented only by a slur at this time. The L wave is rarely difficult to identify; it is usually preceded by a small negative wave which has been termed $L_o$. This was included in the time measurements because it seemed to bear a close temporal relationship to the onset of the 2nd heart sound.

In some acceleration records the identity of the major waves presented difficulty and this was usually due to the presence of waves with multiple tips, the J wave being most frequently affected, the I less often. When there was one dominant tip, this was taken as the major wave for measurement purposes; when there were two or more tips of approximately equal magnitude, an average value was taken.

In acceleration records the width of the I and J waves was measured at the baseline; these are referred to as $I_t$ and $J_t$, respectively. In velocity records similar measurements are referred to as $'I_t$ and $'J_t$.

### (3) *Amplitude*

In the acceleration records obtained during *normal breathing* one or two complete typical respiratory cycles were selected and the amplitude of the major waves measured in each of the 7–10 complexes inscribed during this interval. The values for each wave were averaged and then converted to absolute units. For convenience, milli-G (mG) was the unit used; 1 mG (0.001G) is approximately equal to 1 cm/-sec². The average cycle length during this interval was determined and pulse rate was calculated.

In each of the three *suspended respiration* records three or four typical cycles were selected and the amplitudes of displacement, velocity, and acceleration waves were measured separately and averaged. After conversion to absolute units the amplitude values for all three respiratory

positions were averaged. Approximately 6 to 8 cycles were used to estimate mean cycle length and pulse rate.

In each subject mean amplitude values were expressed in acceleration, velocity and displacement units; multiplication by the mass of body + platform then gave values in terms of force, momentum, and mass-displacement of the body, respectively.

*(4) Mean Time and Amplitude Values*

Mean values for the time and amplitude measurements were determined for each of the four groups of normal subjects. Differences between the 3rd and 4th decade means in males and between the 3rd and 4th decade means in females were determined. Two means were considered significantly different if the difference between them were greater than twice the standard error of the difference; that is, if the ratio, d/S.E. were greater than 2.

The two age decades were combined in each sex to give mean values for males 20 to 39 and females 20 to 39 years. The significance of the differences between the two groups was determined.

## Normal Displacement, Velocity, and Acceleration Ballistocardiograms

### (A) characteristics and variability of waveform

*(1) Head-Foot Ballistocardiograms*

This presentation will be concerned only with the D, V, and A records obtained during *suspended respiration*. The nature of the acceleration ballistocardiograms recorded during normal breathing will be the subject of a subsequent report.

The records shown diagrammatically in Figure 1 were based on the mean time and amplitude measurements from 25 men 20 to 29 years of age; they are composites of the waveform features of the whole group. The general character of the D, V, and A records of this type has been briefly commented on and their intrinsic relationship described elsewhere.[11]

In *displacement* records the major events represented are: a sizable footward movement of the body (″I to ″J) during early systole, a larger and longer headward displacement (″J to ″M) during late systole, reversal of direction (″M) and footward motion (″M to ″N) in early diastole, followed by a more gradual return to the point of origin during the remainder of diastole.

The waveform of the displacement record varies considerably from one person to the next, as is illustrated by the records in Figures 2 and 3 from normal subjects. The complexes in A and C of Figure 2 represent extremes, while those in Figures 2B and 3 are more typical in form. The points ″I, ″J, and ″M can be distinguished in all normal displacement records. In most cases ″M is a reasonably sharp bend; in these the point of maximum headward displacement coincides with the point of maximum curvature. (In some, with flattened or irregular tips, these points may not coincide.) ″N may be sharp or indistinct. The later diastolic part of the tracing may be quite variable but most commonly it descends gradually. In some records, especially those taken at end-inspiration, this descent is temporarily interrupted in presystole by a slow, rounded wave (labeled ″G in Figures 1 and 4). Shortly after the onset of ventricular systole there is a reversal of direction at ″H and a small headward displacement (″H to ″I) ending at ″I. It should be noted in Figure 1 that the tips of the major displacement and acceleration waves, though opposite in direction, coincide approximately in time;* at these points velocity is zero.

In *velocity* records the initial systolic wave is the small headward ′H, followed by the footward ′I. ′J is usually broad and rounded. Between ′J and ′M there is a notch or flexure, ′L, which is temporally related to the end of systole; it is usually, but not always, above the baseline. ′M is a small footward diastolic wave (see Figures 1–3).

The *acceleration* record shows even more individual variability than the other two (see Figures 2–4). The waveform of the Starr and Dock records is rather simple and consistent from one person to the next; this consistency is mainly due to the consistency of the "dorsal springs" of different individuals. The ultra-

* In Figure 1 the corresponding wave tips are not exactly synchronous for reasons given in the Appendix.

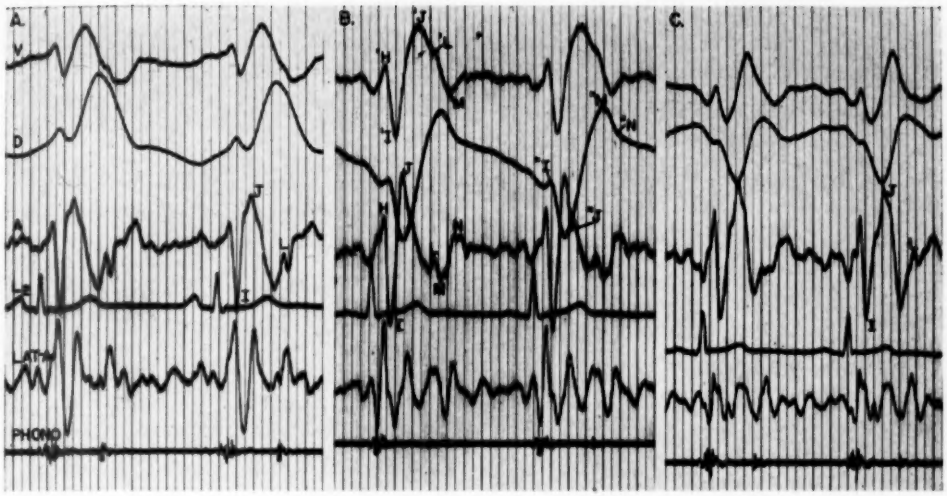


Fig. 2. Normal ULF ballistocardiograms from three young males. These illustrate individual differences in waveform; the records in B are rather typical in waveform whereas those and A and C represent extremes. LAT-A refers to the lateral acceleration record; rightward is upward. In these and all other photographic reproductions of records, paper speed was 5.0 cm/sec and time lines are 0.1 sec apart. In all illustrations the ballistocardiograms were recorded with respiration suspended.

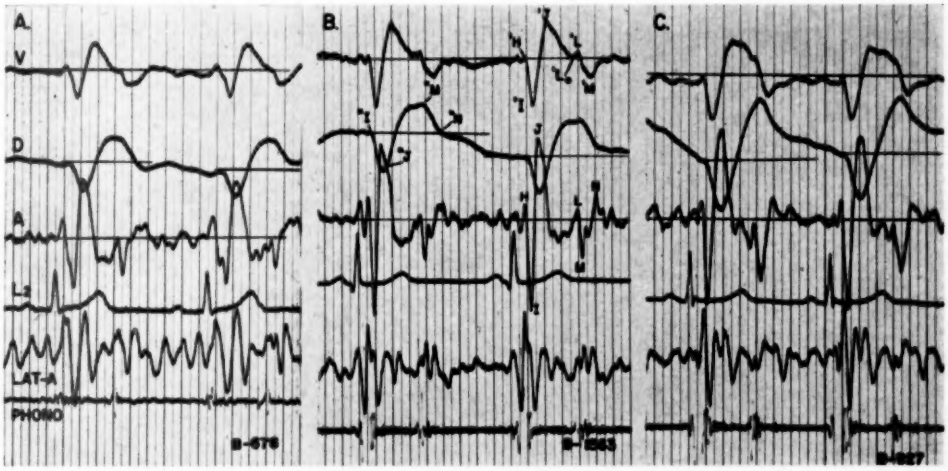


Fig. 3. Normal ULF ballistocardiograms from three young females. Baselines are drawn in to indicate the manner in which they are placed. See text.

low frequency systems minimize or eliminate the influence of the dorsal spring and thereby eliminate the artifactual consistency of waveform. The counterparts of the H, I, J, L, M, and N of the Starr record are represented in the ULF acceleration record but are earlier in time, more variable in pattern and contain faster detail. A more comprehensive comparison of these two types of records has been reported elsewhere.[14]

The major systolic waves of the acceleration record are the H, I, and J. The beginning of the H wave upstroke is frequently marked by a small negative wave or flexure (labeled $H_o$ in Figure 1) which approximately coincides with the onset of the 1st heart sound. H is a sharp, small, headward wave with its tip about 0.05 sec after the beginning of the 1st heart sound. It is usually discrete but is occasionally split or notched. Small secondary waves or slurs on the HI segment are common. The large, footward I wave may have a single sharp tip or may

be slightly split or rounded. Slurs or small secondary waves on the IJ segment are frequent. The large headward J wave falls in mid-systole and is approximately equal to the I wave in amplitude. This wave is quite variable but most commonly there is a single dominant peak with small secondary peaks or slurs before and/or after it; there may be as many as three peaks approximately equal in height. The J downstroke is irregular and variable.

Preceding the tip of the L wave a small negative wave or slur, $L_o$, can often be identified; it bears a close temporal relationship to the initial vibration of the 2nd heart sound and therefore serves to mark the end of ventricular systole. L, M, and N are diastolic waves. L is a small, sharp wave with its tip directed upward and falling either above or below the baseline. It is followed by the footward M wave. A pair of secondary waves are present in most cases between M and N. The N wave is irregular and variable.

When the displacement records shows a reasonably distinct "G wave, there is often a triphasic complex of waves in the acceleration record in presystole. Synchronous with the beginning, peak, and end of the "G wave are the small positive, negative, and positive waves, labeled $F_1$, G, and $F_2$ in Figure 1. These are so variable and indefinite that special designation is probably not justified. Attention is called to them because they will be referred to subsequently in a consideration of the contribution of atrial contraction to the ballistocardiogram.

There are differences in the waveform of the D, V, and A records in the three respiratory positions but these are not usually large.

If a single record could be taken instead of three, i.e., D, V, and A, the time and equipment required would be greatly reduced. The three aspects of motion are related in an exact way mathematically, and from any one the other two can be derived electronically. In practice, however, it has not been possible to predict from any one record the waveform of the other two with any accuracy. Two acceleration records may appear quite similar but the corresponding displacement records may be decidedly different. The attenuation of high frequency information in displacement and of low frequency information in acceleration is so great that electronic derivation or separate recording is required if all the available information is to be obtained.

### (2) *Lateral (Side-to-Side) Ballistocardiograms*

For reasons to be given, these records will be accorded only brief consideration. The convention for polarity used was that officially recommended;[11] leftward motions are represented by negative or downward deflections on the records. There is, as yet, no nomenclature for the waves of the lateral records.

In lateral *acceleration* records (see Figures 2–4) there is, superficially at least, greater variability in waveform than is present in head-foot records, and the waves of the two records are only occasionally in phase. There are usually two or three groups of waves in the lateral, one in early and mid-systole, one in early diastole, and in some cases there is a group in presystole.

The lateral *displacement* records are much less variable in waveform than might have been expected from the acceleration records. A typical tracing is shown in Figure 4. In general the body's motion is leftward during systole and rightward during diastole. In systole, as

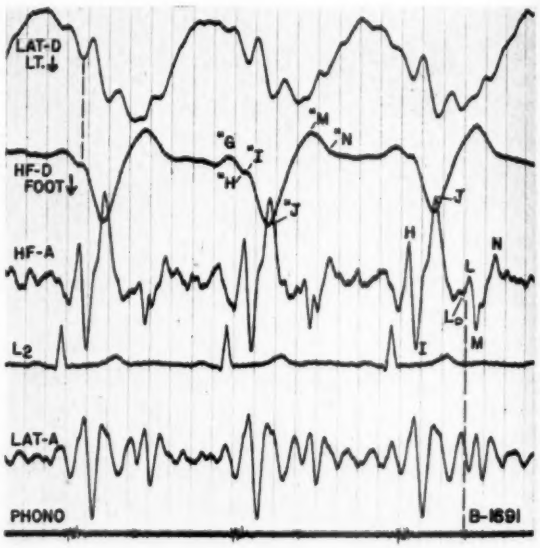


Fig. 4. Simultaneous head-foot displacement (HF-D) and acceleration (HF-A) records and lateral displacement (LAT-D) and acceleration (LAT-A) records. From a young normal female. Polarity of the tracings is indicated by the arrows. See text.

the body begins to move footward, there is a transient rightward motion followed by a larger leftward displacement. A transient reversal takes place shortly after "J. Beginning at about the "M peak the body moves rightward until late diastole. It should be remembered that motions of body and blood are in opposite directions.

The lateral records from all ULF ballistocardiographic systems now in use are of questionable validity because they are probably mixtures of translational and rotational motion, and if this be true they cannot legitimately be combined with the head-foot record (pure translation) to determine frontal plane motion. Talbot[15] anticipated this difficulty for reasons given elsewhere. In an attempt to determine experimentally the relative quantity of translation and rotation in the lateral ballistocardiogram, these were recorded with the subject in the supine and prone positions in a sizable group of young persons. If the lateral record is mainly translation, then its polarity should be reversed in the prone position; if it is mainly rotation, the polarity should be unchanged. Preliminary results[16] suggest that these lateral records represent a mixture of both types of motion. No records have been obtained thus far from a suspension which eliminates this roll artifact.

### (B) TIME AND AMPLITUDE MEASUREMENTS FROM NORMAL D, V, A BALLISTOCARDIOGRAMS

#### (*1*) *Time Measurements*

The mean values from 50 males and 50 females 29–39 years of age are contained in Tables I–III. Statistical treatment of these data has not been completed and they will not be discussed in detail here. However, there are several points which deserve comment.

An atrial heart sound ($S_a$) was present in 37 of the 100 subjects. Its onset preceded the Q wave of the ECG by about 0.05 sec and followed the beginning of the P wave by about 0.11–.12 sec. This sound usually falls about the middle of the displacement "G wave as Figure 1 shows.

The onset of the 1st heart sound occurred about 0.058 sec after the Q wave and the acceleration points $F_2$ and $H_o$ fall in the same region, being about 0.050 and 0.069 sec after the Q wave, respectively. The tips of the 'H and H waves were somewhat later in time.

The mean values for the interval Q-$S_2$ were surprisingly similar in the four groups although there were moderate differences in cycle length. The onset of $S_2$ and the acceleration wave $L_o$ were almost identical in time, while 'L and L occurred somewhat later.

A 3rd heart sound ($S_3$) was present in 56 of the 100 subjects. The interval between the Q wave and its onset averaged about 0.53 sec; the mean interval between the onsets of $S_2$ and $S_3$ was about 0.14 sec. There seemed to be a definite relation between $S_3$ and both "N and N although the onset of $S_3$ occurred slightly earlier in time. In point of time, $S_3$ is generally considered to mark the end of the rapid filling phase of ventricular diastole.

The mean duration of ventricular systole, determined from the onsets of $S_1$ and $S_2$, was almost identical in the four groups, ranging from 0.325 to 0.338. In the acceleration records the points $F_2$ and $H_o$ can be averaged to place the onset of the 1st heart sound in time, and point $L_o$ serves to indicate the onset of the 2nd heart sound; the interval between them is then a rather precise measure of the duration of systole. However, in some cases these points are absent or cannot be identified with certainty, and therefore their use in determining the duration of ventricular systole is limited. The acceleration H and L are usually easy to identify, and the interval between them appears to be clearly related to the duration of systole; the mean values for the latter are slightly greater (by 0.013–.022 sec) than those for the H-L interval. A similar relationship is apparent between the velocity 'H-'L interval and the duration of systole; however, in some records 'L is not sufficiently distinct to permit accurate measurement.

With regard to the relationship between the various time intervals referred to above, a word of caution is in order. The fact that the *mean* values for two time intervals are similar or identical does not mean that they are necessarily related to each other. Possible relationships of this kind should, of course, be tested by calculating correlation coefficients and regressions;

TABLE IV
Amplitude Measurements

| | | Displacement ballistocardiogram | | | | | Velocity ballistocardiogram | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | "IJ | | "JM | | "IJ / "JM | 'I | | 'J | | 'HI | | 'IJ | |
| | | μ | g-cm | μ | g-cm | % | mm/sec | g-m/sec | mm/sec | g-m/sec | mm/sec | g-m/sec | mm/sec | g-m/sec |
| Males | | | | | | | | | | | | | | |
| 20–29 yr | Mean | 39.38 | 320.4 | 92.80 | 763.7 | 42.66 | 0.671 | 54.65 | 0.700 | 57.49 | 0.808 | 66.00 | 1.367 | 111.99 |
| n = 25 | S.D. | 8.95 | 66.5 | 19.70 | 179.8 | 9.26 | 0.127 | 10.43 | 0.147 | 13.33 | 0.143 | 11.48 | 0.225 | 19.38 |
| Males | | | | | | | | | | | | | | |
| 30–39 yr | Mean | 36.08 | 298.4 | 80.80 | 680.2 | 46.18 | 0.646 | 54.12 | 0.613 | 51.78 | 0.758 | 63.56 | 1.258 | 105.78 |
| n = 25 | S.D. | 11.27 | 104.8 | 23.57 | 213.9 | 15.32 | 0.171 | 15.36 | 0.100 | 11.90 | 0.171 | 16.39 | 0.200 | 21.68 |
| Males | | | | | | | | | | | | | | |
| Difference (d) in means | | 3.30 | 22.0 | 12.00 | 83.5 | −3.52 | 0.025 | 0.530 | 0.087 | 5.71 | 0.050 | 2.44 | 0.109 | 6.21 |
| | d/S.E. | 1.15 | 0.87 | 0.95 | 1.35 | 0.98 | 0.59 | 0.14 | 0.77 | 1.61 | 1.11 | 0.61 | 1.84 | 1.05 |
| Females | | | | | | | | | | | | | | |
| 20–29 yr | Mean | 29.22 | 189.0 | 78.00 | 507.9 | 36.25 | 0.487 | 32.33 | 0.611 | 39.66 | 0.568 | 36.64 | 1.113 | 72.12 |
| n = 25 | S.D. | 9.58 | 63.6 | 19.15 | 144.4 | 8.62 | 0.153 | 8.39 | 0.101 | 7.99 | 0.120 | 7.98 | 0.202 | 15.13 |
| Females | | | | | | | | | | | | | | |
| 30–39 yr | Mean | 23.88 | 159.0 | 59.67 | 398.7 | 43.34 | 0.480 | 31.89 | 0.536 | 35.66 | 0.575 | 38.28 | 1.016 | 67.58 |
| n = 25 | S.D. | 6.71 | 50.9 | 13.15 | 105.3 | 14.20 | 0.108 | 8.19 | 0.106 | 8.02 | 0.115 | 9.27 | 0.175 | 13.72 |
| Females | | | | | | | | | | | | | | |
| Difference (d) in means | | 5.34 | 30.0 | 18.33 | 109.2 | −7.09 | 0.007 | 0.44 | 0.075 | 4.00 | −.007 | −1.64 | 0.097 | 4.54 |
| | d/S.E. | 2.27 | 1.84 | 3.87 | 3.06 | 2.14 | 0.18 | 0.19 | 2.56 | 1.77 | 0.21 | 0.67 | 1.84 | 1.11 |
| Males | | | | | | | | | | | | | | |
| 20–39 yr | Mean | 37.73 | 309.4 | 86.80 | 722.0 | 44.41 | 0.659 | 54.39 | 0.657 | 54.64 | 0.783 | 64.78 | 1.313 | 108.89 |
| n = 50 | S.D. | 10.33 | 88.51 | 22.5 | 225.4 | 12.83 | 0.152 | 13.15 | 0.130 | 12.94 | 0.161 | 14.19 | 0.224 | 20.81 |
| Females | | | | | | | | | | | | | | |
| 20–39 yr | Mean | 26.55 | 174.0 | 68.84 | 453.3 | 39.80 | 0.484 | 32.11 | 0.574 | 37.66 | 0.572 | 37.46 | 1.065 | 69.88 |
| n = 50 | S.D. | 8.70 | 59.4 | 18.80 | 130.8 | 12.23 | 0.131 | 8.29 | 0.102 | 8.24 | 0.116 | 8.61 | 0.192 | 14.46 |
| Total male and female | | | | | | | | | | | | | | |
| Difference (d) in means | | 11.18 | 135.4 | 17.96 | 268.7 | 4.61 | 0.175 | 22.28 | 0.083 | 16.98 | 0.211 | 27.32 | 0.248 | 39.01 |
| | d/S.E. | 5.85 | 9.00 | 4.33 | 7.30 | 1.87 | 6.20 | 10.15 | 3.53 | 7.82 | 7.50 | 11.60 | 5.95 | 10.90 |

μ = microns; g-cm = gram-centimeter; $\frac{\text{g-m}}{\text{sec}}$ = gram-meters/second.

this work is in progress but is not yet complete. Nevertheless, there is good reason for believing that the relationships mentioned will be statistically significant.

Elsbach[13] called attention to the relationship between the 1st heart sound and the tips of the 'H and H waves and between the 2nd sound and the 'L and L wave tips.* He found that there was a statistically significant correlation between duration of systole ($S_1$-$S_2$) and the intervals H-L and 'H-'L. The significance of this and similar time relationships will be considered below.

*(2) Amplitude Measurements*

Mean amplitude values for the four age and sex groups are contained in Tables IV and V. Table VI contains the data relating to height, weight, surface area and age. A detailed con-

* Elsbach used a system for designating waves in the DVA records differing from that used here. This is mainly a matter of applying different symbols to the same waves or points. His point "p" is not exactly the same as our 'L but corresponds to our $'L_o$, the onset of L or the first definite break in the 'J downstroke. Although we measured $'L_o$ it was often so indefinite as to make this measurement unreliable and for this reason was not included in the tables.

TABLE V
Amplitude Measurements*

| | | Rate per min | Acceleration ballistocardiogram | | | | | | Suspended respiration | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | H | | I | | J | | HI | | IJ | | MN | |
| | | | mG | g | mG | g | mG | g | mG | g | mG | g | mG | g |
| Males | | | | | | | | | | | | | | |
| 20–29 yr | Mean | 63.8 | 1.18 | 97.4 | 2.87 | 234.6 | 3.04 | 249.8 | 4.04 | 332.0 | 5.93 | 485.8 | 2.71 | 221.9 |
| n = 25 | S.D. | 9.0 | 0.42 | 37.5 | 0.64 | 53.8 | 0.50 | 46.7 | 0.88 | 79.3 | 0.93 | 82.9 | 0.57 | 51.9 |
| Males | | | | | | | | | | | | | | |
| 30–39 yr | Mean | 67.2 | 1.09 | 90.6 | 2.58 | 217.7 | 2.72 | 228.5 | 3.64 | 305.7 | 5.29 | 445.6 | 2.34 | 198.8 |
| n = 25 | S.D. | 8.2 | 0.31 | 27.3 | 0.56 | 57.7 | 0.51 | 50.8 | 0.73 | 69.6 | 0.90 | 96.9 | 0.63 | 61.0 |
| Males | | | | | | | | | | | | | | |
| Difference (d) in means | | −3.4 | 0.09 | 6.8 | 0.29 | 16.9 | 0.32 | 21.3 | 0.40 | 26.3 | 0.64 | 40.2 | 0.37 | 23.1 |
| | d/S.E. | 1.40 | 0.81 | 0.73 | 1.70 | 1.07 | 2.27 | 1.55 | 1.77 | 1.25 | 2.46 | 1.58 | 2.16 | 1.44 |
| Females | | | | | | | | | | | | | | |
| 20–29 yr | Mean | 69.7 | 0.84 | 54.6 | 2.16 | 139.4 | 2.61 | 168.5 | 3.01 | 194.2 | 4.79 | 309.8 | 2.62 | 168.7 |
| n = 25 | S.D. | 10.2 | 0.34 | 21.0 | 0.60 | 41.0 | 0.72 | 52.6 | 0.83 | 54.8 | 1.27 | 88.9 | 0.73 | 37.1 |
| Females | | | | | | | | | | | | | | |
| 30–39 yr | Mean | 72.5 | 0.76 | 50.7 | 2.31 | 152.7 | 2.80 | 186.0 | 3.08 | 204.1 | 5.10 | 337.9 | 2.42 | 160.4 |
| n = 25 | S.D. | 8.2 | 0.36 | 26.3 | 0.62 | 42.0 | 0.67 | 50.2 | 0.82 | 58.1 | 1.15 | 83.7 | 0.59 | 44.8 |
| Females | | | | | | | | | | | | | | |
| Difference (d) in means | | −2.8 | 0.09 | 3.9 | −0.15 | −13.3 | −0.19 | −17.5 | −0.07 | −9.9 | −0.31 | −28.1 | 0.20 | 8.3 |
| | d/S.E. | 1.07 | 0.88 | 0.57 | 1.42 | 1.14 | 0.99 | 1.66 | 0.30 | 0.62 | 0.13 | 1.15 | 1.06 | 0.71 |
| Males | | | | | | | | | | | | | | |
| 20–39 yr | Mean | 65.3 | 1.13 | 94.0 | 2.72 | 226.2 | 2.88 | 239.2 | 3.84 | 318.8 | 5.61 | 465.7 | 2.53 | 210.4 |
| n = 50 | S.D. | 8.8 | 0.39 | 33.0 | 0.63 | 56.3 | 0.54 | 49.7 | 0.71 | 76.0 | 0.97 | 92.3 | 0.61 | 57.5 |
| Females | | | | | | | | | | | | | | |
| 20–39 yr | Mean | 71.1 | 0.80 | 52.6 | 2.23 | 146.0 | 2.70 | 177.3 | 3.04 | 199.2 | 4.94 | 323.8 | 2.52 | 164.5 |
| n = 50 | S.D. | 9.4 | 0.37 | 24.0 | 0.62 | 42.5 | 0.72 | 51.0 | 0.84 | 56.6 | 1.23 | 166.4 | 0.65 | 47.1 |
| Total male and female | | | | | | | | | | | | | | |
| Difference (d) in means | | −5.8 | 0.33 | 41.4 | 0.49 | 80.2 | 0.18 | 61.9 | 0.80 | 119.6 | 0.67 | 141.9 | 0.01 | 45.9 |
| | d/S.E. | 1.75 | 4.38 | 7.17 | 3.96 | 8.05 | 1.42 | 6.05 | 5.13 | 8.94 | 3.03 | 5.27 | 0.79 | 4.37 |

* mG = milli-G (unit of gravitational acceleration); g = force in grams.

sideration of the amplitude measurements will be reported at a later date and only a few general points will be touched on here.

In either sex, the subjects in the two age groups were comparable in height, weight, and surface area. Differences in mean values exist but are not significant. As expected, the mean values are significantly higher in the males than in the females.

*Comparison of Mean Amplitude Values for the Two Age Groups in Either Sex:* In *males* the mean values for wave amplitude in the three types of records are, without exception, larger in the younger group than in the older. On the other hand, with but few exceptions, these differences are not large enough to be considered statistically significant. Nevertheless, these findings probably reflect a real trend of BCG amplitude to decrease with age for it is highly unlikely that the amplitude values would be so consistently larger in the younger men as a result of chance alone. If the age span were increased, this trend might become clearly manifest. In an earlier study[17] based on records from the high-frequency bed, a highly significant negative correlation was found to exist between BCG amplitude and age.

TABLE VI

Age, Weight, Height and Surface Area

| | | Height (inches) | Body weight (kg) | Body + platform weight (kg) | Surface area ($M^2$) | Age (yr) |
|---|---|---|---|---|---|---|
| Males | | | | | | |
| 20–29 yr | Mean | 70.97 | 75.39 | 82.19 | 1.928 | 25.5 |
| n = 25 | S.D. | (6.28) | (9.20) | (9.20) | (0.1313) | (2.6) |
| Males | | | | | | |
| 30–39 yr | Mean | 70.46 | 77.12 | 83.92 | 1.929 | 33.7 |
| n = 25 | S.D. | (2.08) | (10.83) | (10.83) | (0.142) | (2.7) |
| Males | | | | | | |
| Difference (d) in means | | +0.512 | −1.724 | −1.724 | −0.0012 | −8.2 |
| | d/S.E. | 0.79 | 0.61 | 0.61 | 0.003 | 11.1 |
| Females | | | | | | |
| 20–29 yr | Mean | 65.16 | 58.02 | 64.82 | 1.625 | 23.1 |
| n = 25 | S.D. | (2.36) | (7.72) | (7.72) | (0.1223) | (2.8) |
| Females | | | | | | |
| 30–39 yr | Mean | 65.05 | 59.94 | 66.74 | 1.645 | 34.5 |
| n = 25 | S.D. | (2.45) | (8.85) | (8.85) | (0.140) | (3.1) |
| Females | | | | | | |
| Difference (d) in means | | +0.112 | −1.928 | −1.928 | +0.003 | −11.4 |
| | d/S.E. | 0.16 | 0.82 | 0.82 | 0.08 | 13.7 |
| Males | | | | | | |
| 20–39 yr | Mean | 70.72 | 76.25 | 83.05 | 1.929 | 29.6 |
| n = 50 | S.D. | (2.32) | (10.15) | (10.15) | (0.137) | (4.8) |
| Females | | | | | | |
| 20–39 yr | Mean | 65.12 | 58.98 | 65.78 | 1.635 | 28.8 |
| n = 50 | S.D. | (2.41) | (8.36) | (8.36) | (0.132) | (7.1) |
| Total males and females | | | | | | |
| Difference (d) in means | | +5.608 | +17.274 | +17.274 | +0.2936 | +0.8 |
| | d/S.E. | 11.89 | 9.34 | 9.34 | 10.92 | 0.66 |

In *females* the differences between the two age groups are less consistent than in men. In almost all measurements from displacement and velocity records, the mean values are greater in the younger age group. While the differences in mean amplitude values are significant for most displacement measurements, they are not for the majority of the measurements from velocity records. Unlike the results obtained in the males, the mean amplitudes of the major acceleration waves or segments (I, J, HI, and IJ) are consistently (but not significantly) greater in the older group of females.

In both males and females, differences in mean amplitude values for the two age groups are either not significant, or if so, not very great. This made it possible to combine the two groups and compute means for the 50 males 20–39 years and for the 50 females 20–39 years.

*Comparison of Mean Amplitude Values for the Two Sexes:* There are large and highly significant differences between the mean values of the two sexes (20–39 years) for all mass-displacement, momentum and force measurements. Since these were computed by multiplying the magnitude of the platform motion by body plus platform mass, it is hardly surprising that the values were greater for the males, who weighed about 17 kg more than the females.

A rather unexpected finding was that the mean amplitude values for displacement, velocity, and acceleration, with no mass factor included, were also consistently greater in the males. The differences between the means were significant for all measurements except

for the acceleration J wave and MN segment. It is possible to make a correction in the amplitude values to eliminate the influence of platform weight; this takes the following form:

$$\text{Corrected amplitude} = \text{measured amplitude} \times \frac{\text{body} + \text{platform weight}}{\text{body weight}}$$

The figures in Tables IV and V were not corrected in this manner. If the means are corrected by this factor, they are increased 9.0 per cent in men and 11.5 per cent in women but this produces no substantial reduction in the differences between the two sexes. The explanation for this discrepancy is uncertain at present, but it may relate to body size or habitus for which some additional correction may be necessary. Statistical analyses now in progress may prove a suitable explanation.

In his 1905 report[2] Yandell Henderson gave the absolute measurements from displacement records obtained from a number of normal subjects. A comparison of his figures with ours is of interest. In Henderson's data* the mean values from eight normal subjects in their twenties (most of whom were males) were as follows: $''IJ = 37.8\ \mu$, $''JM = 100.0\ \mu$ and $''IJ/''JM = 39$ per cent. The corresponding figures for our 20–29-year-old males are: $''IJ = 39.4\ \mu$, $''JM = 92.8\ \mu$ and $''IJ/''JM = 43$ per cent. All factors considered, these two sets of figures are surprisingly similar. In one subject 48 years of age he found displacement amplitudes only about one-half those of the younger subjects; $''IJ$ was 15.1 $\mu$ and $''JM$ was 48 $\mu$. He observed that, without exception, the curves from young men of athletic habits and more than ordinary muscular development are of considerable size, but those from women and from men of sedentary habits and slight muscular development are notably small. Honig and Tenny[35] recently reported the results of force measurements from (ULF) acceleration ballistocardiograms obtained on males and females ranging in age from $2^1/_2$ to 87 years. Their findings merit attention and will be discussed and compared with our results elsewhere.

* Henderson's figures were corrected for platform weight; the correction was eliminated in order to compare them with ours.

## Some Determinants of the ULF Ballistocardiogram: Physical Aspects of the Circulation

The term "cardiovascular generator" will be used here to include the heart and all the vessels (arteries and veins) in which significant mass motions take place. This "generator" is connected to the rest of the body by elastic couplings whose mechanical characteristics have not been determined experimentally, mainly because of technical difficulties. The elastic couplings of the "generator" may alter the relationship between the mass-motions of the blood and the body so that a high-cut filter effect is produced. Probably the largest source of distortion arises from the connections of the heart and ascending aorta to the body, for they appear to be bound down less firmly than is the rest of the generator. Von Wittern[b] and Burger[18] have sought to determine the nature and magnitude of the errors from this source but the question remains unsettled. In any case, since the internal coupling network behaves like a high-cut filter (which, in this case, may have a resonance peak at its corner frequency), one may predict that the main effect will be upon the faster motions, as in the acceleration records, and that the effect on the slower motions reflected by the displacement record will be small or negligible.

For the purposes of this discussion the internal coupling network will be ignored, and it will be assumed that the mass-motions of the body recorded with an ULF system accurately reflect, with opposite sign, the internal mass-motions of the blood.† Employing mass-motion terms, the displacement, velocity, and acceleration records from these systems provide a measure of the mass-displacement, momentum, and force of body and blood, respectively. Records of mass-motion in the longitudinal (head-foot) axis represent the algebraic sum

† The internal mass involved is not only that of the blood but also includes any other mass, e.g. the heart itself, which is set into motion as a consequence of the pumping and circulation of blood.

of all mass-motions within the circulatory system along this axis; they therefore reflect changes in the center of gravity of the total blood mass. If mass-motions in different parts of the circulation are equal in magnitude but opposite in direction, there is cancellation and no change in center of gravity; this is, of course, an important consideration in the human circulatory system since blood flows away from and returns to the heart simultaneously.

If the circulatory system through which the heart pumps blood were a closed circuit of indistensible tubes, the algebraic sum of mass-motions would always be zero, there would be no change in the blood's center of gravity, and no external body motion (the ballistocardiogram) would be produced. This would be true regardless of the size and configuration of the "circulatory system," stroke volume, velocity of blood flow, blood pressure or peripheral resistance. In the human circulatory system these factors assume importance because the distensibility of the vessels permits changes in the mass distribution and center of gravity of blood. The human displacement ballistocardiogram is, in a sense, a whole body plethysmogram, or an algebraic sum of simultaneous plethysmograms of all vessels (multiplied by their distances from the heart) inscribed continuously throughout the cardiac cycle. The first and second derivatives of this summated plethysmogram correspond to the velocity and acceleration ballistocardiograms.

It is, of course, impossible to take simultaneous plethysmograms from all vessels, but Noordergraaf[19,20] recently used this general approach with considerable success in deriving the human ballistocardiogram.* Using anatomic measurements, an average value for arterial distensibility, and a normal central blood pressure and pressure pulse contour, he calculated the uptake of blood by successive segments of all the major arteries and plotted them with respect to time. The uptake curve for each segment was multiplied by its distance from the heart and then these were summated algebraically. The resulting summated uptake curve, and its first and second derivatives, were surprisingly similar to the ULF displacement, velocity, and acceleration ballistocardiograms with respect to both waveform and magnitude. His calculations did not include the effect of movement of blood within the veins, for he believed this to be small. The pulmonary arterial circulation was included, but compared to the systemic circulation its contribution proved to be relatively minor. His derived displacement curve showed counterparts of the "J, "M, and "N waves of the normal ballistocardiogram but the "G and "H waves were not represented and the "I wave is probably not comparable to his. The "JM amplitude of his derived curve is almost identical with the mean "JM amplitude (about 720 g-cm) of the displacement ballistocardiograms from our males 20–39 years.

Much earlier Hamilton and his associates[21] approached the problem in much the same way but used somewhat different methods. They derived a summated force curve from calculated forces arising in the heart, aorta and pulmonary artery. The waveform of this curve is surprisingly similar to that of normal force (acceleration) ballistocardiograms from ULF systems and it shows two diastolic waves which seem to correspond to the L and M waves.

The mass-motions of the human body can be broken down into mass and motion components since these may be measured separately. However, while the product, mass motion, of the blood can be measured, the mass and motion of the blood have not been quantitated separately. If a human body with a mass of 70 kg is displaced 10 $\mu$, the product, 700 g-cm, will be equal to the mass-displacement of blood (with opposite sign). This value could result from the movement of 100 g of blood a distance of 7 cm or of 50 g of blood 14 cm, or any other combination yielding the same product. Similarly, the momentum and force of the blood can be approximated but neither the mass nor the motion (velocity and acceleration) of the blood has been measured separately.

### DIRECTION AND DISTRIBUTION OF BLOOD FLOW

The circulatory system is shown schematically in Figure 5 to illustrate the direction and distribution of blood flow in the human body. The systemic arterial system is in black, the

* His full report will be published in the Dec. issue.

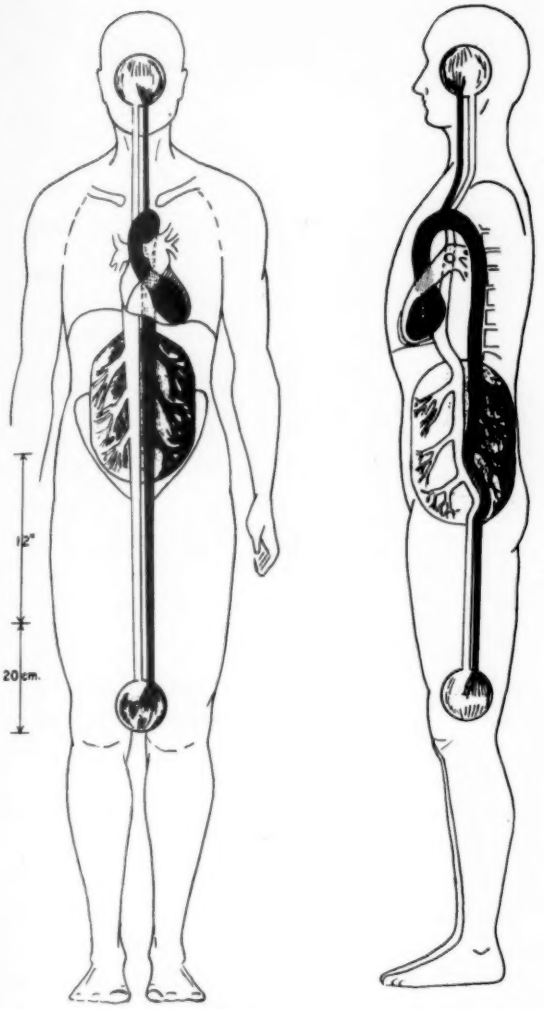


Fig. 5. Diagram of the circulation to represent direction and distribution of blood flow. The systemic arterial system is in black, the venous and pulmonary arterial system in white. The size and shape of the cardiac chambers and intra-thoracic vessels were based on angiocardiographic measurements.[33,34] Estimated distribution of blood flow to various parts of the body is represented by round or ovoid "lumped" vascular beds. See text.

venous and pulmonary arterial systems in white.

*Systemic Arterial System:* In the systemic arterial system, all of the blood ejected by the left ventricle (excluding that to the coronary tree) moves headward from the mid-left ventricle to the aortic arch, a distance of approximately 10–12 cm. Beyond the arch only about 15 per cent of the blood continues to move headward; this is represented by a small circular bed in the head. The remaining 85 per cent of the blood flows footward from the arch and includes the flow through the upper extremities when these are placed alongside the body. In Figure 5 a large systemic vascular bed which represents the proportion of total flow to the truck and upper extremities was placed in the abdomen because this region receives approximately 50 per cent of the cardiac output. An additional small bed was placed at the knees to indicate the estimated distance and relative quantity of blood flow to the lower extremities. This diagram of the circulation could be further simplified by eliminating the head and lower extremity beds and representing the whole systemic circulation as a single lumped bed.

These diagrams can lead to erroneous impressions if consideration is not given to the existence of *arterial distensibility*. If, in Figure 5, the aorta between the left ventricle and the abdominal bed (the two small beds being neglected) were indistensible, then with the onset of ejection there would be an instantaneous footward displacement of blood into the abdominal bed, the effective distance being that between the mid-left ventricle and the midpoint of the bed. The resulting footward mass-displacement of blood would be the product of this distance and the mass of blood transferred. Under these circumstances the rate of uptake (or the blood volume increase) of the abdominal bed would be entirely dependent on the volume rate of ejection by the left ventricle. However, in the human with distensible arteries, when blood is ejected by the left ventricle it moves not only axially but also radially, so that there is progressive distension of successive arterial segments. The rate at which the waves of distension move from the root of the aorta peripherally over the aortic tree is a function of the "relative" distensibility (which includes the blood pressure factor) of the vessel and can be roughly approximated by the pulse wave velocity. The arrival of the pulse wave in an artery can be taken as an index of the beginning of distension, while maximum uptake occurs later. Figure 6 shows the time in the cardiac cycle at which the pulse wave arrives in some of the major systemic arteries in a young normal subject; the dis-

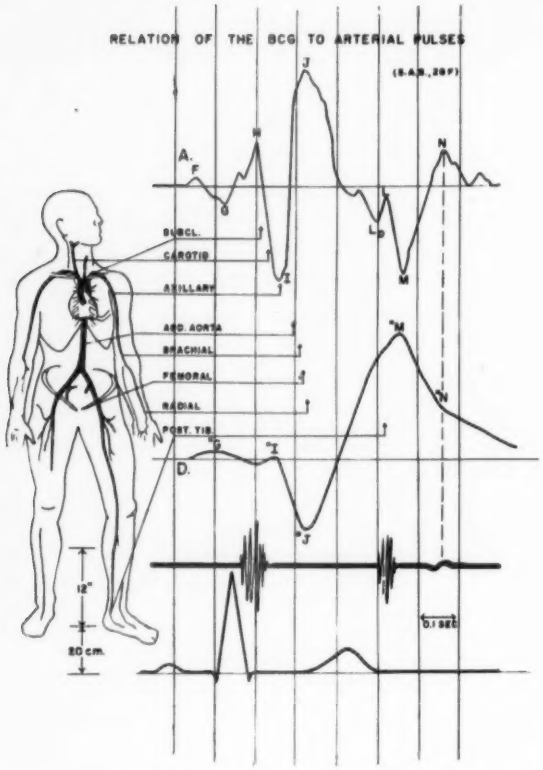


Fig. 6. Diagram showing temporal relationship between ULF ballistocardiograms and pulse wave arrival time in the major system arteries. From a normal 28-year-old female. The arrows indicate the time in the cardiac cycle at which the pulse wave appears in the arteries. Aortic pulse wave velocity (subclavian to femoral) in this subject was approximately 4.0 meters/sec. Note that by the time of the reversal at "J and J the pulse wave has already reached the femoral artery. However, maximum uptake of blood by an artery lags considerably the arrival of the pulse wave. See text.

placement and acceleration ballistocardiograms from the same person are shown in order to indicate temporal relationships. It will be noted that the pulse wave has already reached the femoral artery by the time the "J and J waves are inscribed.

As a consequence of arterial distensibility, with the onset of left ventricular ejection blood is discharged headward and there is progressive distension of the proximal vessels producing an initial headward shift in the blood's center of gravity. As aortic distension progresses beyond the arch and down the descending aorta in a footward direction, the initial headward motion of the blood's center of gravity is arrested and reversed, and during the remainder of systole it moves steadily footward. The actual magnitude of the mass-displacements in the systemic arterial system is unknown, for, while it may be assumed that the stroke volume represents the mass involved, there is no way of determining the mean distance over which this mass is displaced.

During diastole, net systemic arterial blood flow would continue in a footward direction but at a much reduced rate. At the same time, as run-off takes place there is a progressive decrease in the excess volume (and mass) in the vascular bed below the heart. The net effect of the redistribution would be a headward return of the blood's center of gravity to or near its point of origin by the beginning of the next cycle. It seems likely that venous return of blood to the heart plays a part in this diastolic

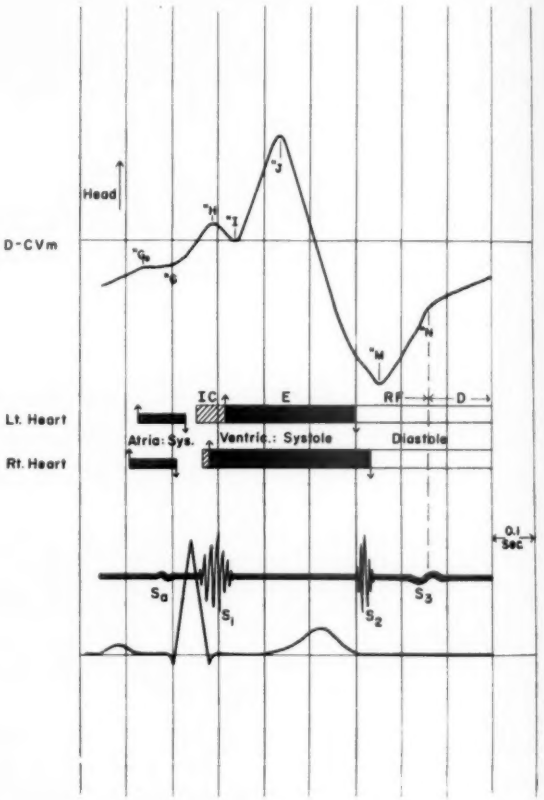


Fig. 7. Diagram of the internal displacement of cardiovascular mass ($CV_m$) and its relation to events in the cardiac cycle. This displacement curve was obtained by inverting and redrawing the body displacement curve of Figure 1. Movement of blood's center of gravity in a headward direction is upward in this figure.

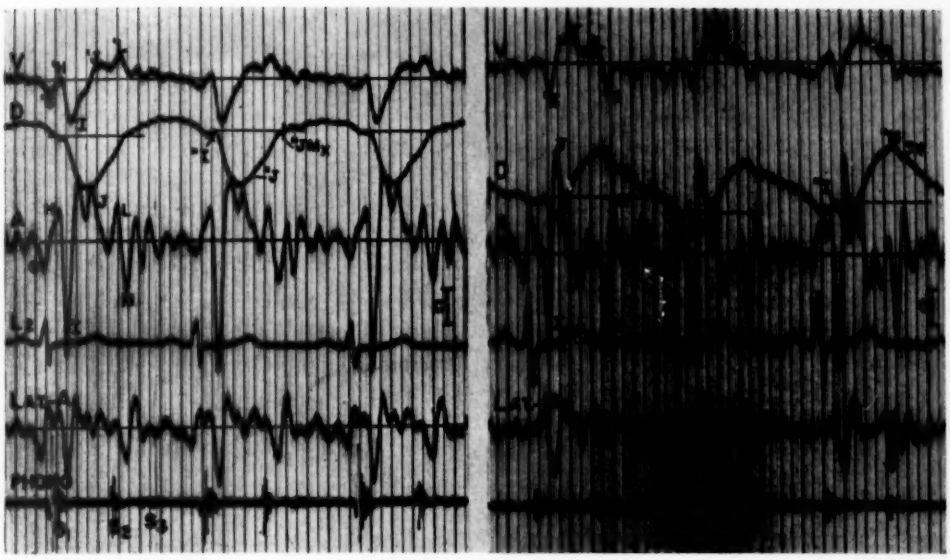

Fig. 8. Pre- and postoperative ULF ballistocardiograms from nine-year-old male with coarctation of the aorta. *Left:* Preoperative records. The most striking alterations are in the displacement record which shows a deep and greatly prolonged footward "J occupying the whole of systole; the normal headward "M is absent. This indicates that the displacement of *blood* during systole is predominantly headward. The normally large and rapid uptake of blood by the vessels distal to the arch cannot take place because of the obstruction and these vessels fill slowly through devious channels. This results in an unbalanced headward displacement of blood-mass during systole. The velocity and acceleration ballistocardiograms are also altered. *Right:* Records taken three weeks after operation. The ballistocardiograms have become normal. In the displacement record the large, broad "J has been replaced by a normal, small "J and this is followed by the large headward "JM displacement. This suggests that the uptake of blood by vessels distal to the arch now takes place normally. The velocity and acceleration records have also become normal.

headward redistribution of blood; the larger flow through the inferior vena cava is assumed to have a dominant effect.

*Pulmonary Arterial System:* The pulmonary circulation differs considerably from the systemic in terms of mass-motion and possesses certain unique characteristics which may eventually permit a reasonable estimate of its contribution to the mass-motions of the circulation as a whole. The bifurcation of the pulmonary artery is approximately in the center of the chest and its branches fan out radially and symmetrically in all directions in such a manner that mass-displacements beyond the bifurcation tend to cancel out one another. This fact provides a finite distance over which a certain mass of blood is effectively displaced during ventricular ejection. If the stroke volume is 80 cc, then by the end of systole an 80 g mass of blood will have been transferred from the mid-right ventricle to the pulmonary artery bifurcation, a distance of about 7 cm in the headward direction. The product of the two represents a mass-displacement of 560 g-cm. This quantity would be reduced by the mass-displacement of the blood returned through the pulmonary veins to the left heart during systole; that this latter may be appreciable is suggested by evidence that blood flow in the pulmonary artery is quite low during diastole, implying that diastolic run-off is probably small.

The displacement ballistocardiogram of Figure 1 is plotted upside down in Figure 7 and represents the internal mass-displacement of blood with proper polarity, headward displacement of blood being inscribed upward in this illustration. The initial headward displacement ("I to "J) may be ascribed to headward shifts of blood in both pulmonary and systemic circulations. Thereafter the mass-displacements in the two circuits are in opposition with some mutual cancellation, but the systemic mass-motions are so dominant that the algebraic sum is a large footward displace-

ment of blood. Partial cancellation probably accounts for the fact that the maximum mass-displacement (mean ″JM in men 20–39 years = 720 g-cm) for the whole circulation was not much greater than that estimated for the pulmonary circulation alone (about 560 g-cm). The evidence suggests that the distribution of blood in the systemic circuit largely determines the ″JM amplitude as well as the relative amplitudes of ″J and ″M. Conditions or procedures which tend to increase the distribution of blood in a headward direction also tend to augment the ″J wave and to diminish the ″M wave. This effect is illustrated in Figure 8 which shows the records obtained from a patient with coarctation of the aorta obtained before and after surgical correction. In the preoperative record (on the left) of *body* displacement there is a deep, prolonged ″J which continues into diastole, and the usual headward ″M is absent; this pattern represents a large, prolonged *headward* mass-displacement of *blood* throughout systole. The normally dominant footward mass-displacement in the arteries distal to the arch is presumably eliminated by the obstruction at the arch and blood flow to regions below it occurs slowly through devious collateral channels. In the records (on the right) obtained after the coarctation was resected, the displacement waveform had become normal with a small ″J and a large ″M.

By contrast, in conditions associated with a greater distribution of blood in a footward direction, ″J is usually attenuated and ″M augmented.[13]

## Relation of ULF Ballistocardiograms to Cardiovascular Events

Reference has already been made to the relation of the heart sounds to normal ULF ballistocardiograms. We have not recorded in man pressures in the heart and great vessels simultaneously with ballistocardiograms. Braunwald and his associates[22] obtained pressure measurements from the two sides of the heart simultaneously (open chest, needle puncture, respiration suspended) on 13 anesthetized men and women without evidence of cardiovascular disease. In Figures 1 and 7 are bar diagrams representing the timing of events in the cardiac cycle for the right and left sides separately; these were based on the Braunwald data and, for the duration of atrial systole, on figures supplied by Wiggers.[23] The conditions under which the pressures and ballistocardiograms were recorded were, of course, quite different; nevertheless, certain similarities in the timing of cardiac events make the two kinds of measurements reasonably comparable.

Interesting differences in the timing of mechanical events on the two sides of the heart in man are evident from Braunwald's data. Contraction of the right atrium begins slightly before that of the left. The onset of ventricular systole is earlier on the left than on the right. However, the isometric phase of ventricular contraction lasts about four times as long for the left ventricle as for the right and as a result ejection of blood into the low-pressure pulmonary artery begins considerably earlier than that into the high-pressure aorta. In addition, the duration of ejection is shorter and the end of systole occurs earlier on the left than on the right. From these relations it appears that the onsets of the 1st and 2nd heart sounds may be taken to indicate the beginning and end of *left* ventricular systole, respectively, and these precede somewhat in time the corresponding events on the right side.

This asynchronous behavior of the two sides of the human heart has since been demonstrated in the dog by Moscovitz and Wilder.[24] The only difference observed was that while in man aortic valve closure precedes pulmonic, in the dog aortic closure very slightly lags pulmonic closure. It has been shown that the normal ULF acceleration ballistocardiogram from the dog resembles rather closely that from man.[25] Ballistocardiograms and central pressures have been recorded simultaneously in a limited number of experiments on dogs. Preliminary results[16] suggest that the general relationship of ballistocardiographic waves to events in the cardiac cycle of the dog is similar to that shown for man in Figure 1.

The discussion to follow will be concerned with our current views regarding the origin of the normal ULF ballistocardiogram of man. Space limitations will not permit the detailed

presentation of evidence in support of these views. It should be emphasized that some of them are conjectural and should by no means be regarded as established facts. A complete and detailed description of the origin of normal and abnormal records will probably not be possible until suitable methods are available for the measurement of instantaneous velocity of blood flow in the great vessels. Until such time inferences will necessarily be based on indirect evidence. It is worth pointing out that in relating ballistocardiographic waves to mechanical cardiovascular events, it cannot be assumed that the existence of a temporal relationship between two events necessarily implies that they are *causally* related.

Since the tips of the waves in displacement and acceleration ballistocardiograms are synchronous in time, though opposite in direction, these records may be conveniently described together; the intermediate velocity record need not be considered here. The BCG records in Figure 1 represent the external motions of the *body* and may be simply inverted to represent internal motion of *blood*, in which case headward motion of blood will be upwards on the paper. In Figure 7 only the displacement record has been so inverted. In order to conserve space, at times the convention for designating displacement and acceleration waves[11] is used; letters preceded by double primes refer to displacement waves and unprimed letters refer to acceleration waves.

### WAVES INSCRIBED DURING PRESYSTOLE

The displacement ″G wave and the acceleration F($F_1$ and $F_2$) and G waves are in presystole. These waves appear to be associated with atrial contraction and bear a consistent relation to the P wave whether AV conduction is normal or not.[13,16] ″G and $F_1$ begin about 0.07 sec after the onset of the P wave and at or near the beginning of the atrial pressure "a" wave.

The variability of the body's displacement ″G wave has already been referred to. In many subjects it is entirely absent, in others it is represented by a change of slope (usually becoming more headward) and in still others it is a rather large, clearly demarcated headward wave. In a given individual it is usually most prominent in records obtained with respiration suspended at end-inspiration, when the heart is oriented in a more longitudinal position. The initial headward and terminal footward ″G displacement of the body should represent displacement of blood at first footward and then headward. With the onset of atrial systole blood is discharged from atria to ventricles in a footward and leftward direction; this forcible discharge very likely displaces the heart's mass in the same direction. The longitudinal component of this mass-displacement should be somewhat increased during held-inspiration. As atrial contraction proceeds from the area of the sinus node, the vena cava junctions (invested with atrial muscle bands) are constricted early, and as blood is "milked" into the ventricles none regurgitates into the cavae. During atrial contraction venous return is temporarily halted and blood is stored in the large central veins. These factors probably account for the initial headward portions of the body ″G wave. By the end of atrial contraction ″G has reached a maximum and this is approximately synchronous with the atrial sound $S_a$. With relaxation blood begins to flow into the atria from the vena cavae. The headward flow through the inferior vena cava would tend to predominate and would account for the final half of the ″G wave.

In addition to the venous contributions to atrial waves it is possible that a small arterial component adds to the initial footward displacement of blood mass. During atrial contraction the reduction in atrial volume is commonly associated with a transient reduction in pressure in the roots of the neighboring aorta and pulmonary artery. This pressure drop could result in some footward displacement of blood into these areas.

The acceleration equivalent of the displacement ″G wave is the triphasic complex labeled $F_1$, G, and $F_2$; these points generally correspond with the beginning, the maximum, and the end of the ″G wave. They are quite variable and often indefinite.

It is of interest that in deriving his displacement, velocity, and acceleration curves Noordergraaf[19,20] did not take into account movement of blood in the veins or motions of the mass

of the heart and these curves do not show presystolic waves (″G, $F_1$, G, and $F_2$).

The displacement ″G tends to blend in with the succeeding negative flexure labeled ″H. Similarly the latter part of the "atrial complex" of the acceleration record tends to mix in with early systolic components.

### WAVES INSCRIBED DURING VENTRICULAR SYSTOLE

The major displacement and acceleration waves during ventricular systole are ″H, ″I, ″J, and H, I, J.

*The HI Segment:* It may be seen in Figure 7 that during early systole the blood's center of gravity reverses directions at ″H and thereafter moves in a footward direction until it again reverses at ″I and moves headward. There is considerable uncertainty about the origin of these early systolic mass motions. The headward ejection of blood from the right ventricle begins at or near the time of the ″H flexure and ejection from the left ventricle begins somewhat later (ca. 0.035 sec), between ″H and ″I. In spite of the fact that blood is being ejected in a headward direction in both of the great vessels, nevertheless the blood's center of gravity moves footward until it reverses at ″I, some 0.025 and 0.06 sec after the onset of ejection from the left and right ventricles, respectively. It appears then that the dominant mass-motions during early systole are footward. Their origin has not been demonstrated conclusively but the explanations offered by Hamilton[21] over a decade ago seem entirely reasonable at this time. He observed a delay in the onset of the I wave of the high frequency bed record from the human when compared with a derived force ballistocardiogram based on events in the arterial system only (aorta and pulmonary artery). He suggested that this was due to cancellation by footward motions of the heart's mass and of venous blood, and that these should begin in isometric contraction and continue for an undetermined period in early systole. They were thought to account in part for the force H wave. Most of the available evidence tends to support these views. With the onset of systole the elongated ventricles become more rounded and spherical and as the atrioventricular septum descends toward the apex, the center of gravity of the heart and the blood within it should move footward. In addition, after the onset of right ventricular isometric contraction the transient bulging of the tricuspid valve into the right atrium which produces a rise in right atrial pressure, the "c" wave, may result in a temporary reflux of blood into the vena cavae, the net effect being footward mass-displacement. While it is true that the velocity of blood flow in the veins is considerably slower than in the arteries, the pressure and capacity characteristics of the venous system are such that relatively small and transient changes in pressure gradient can produce substantial shifts in blood volume within it.

In the acceleration ballistocardiogram (see Figure 1) the H wave tip is synchronous with the displacement ″H* and its amplitude is a measure of the curvature at ″H. The Braunwald data indicate that right ventricular ejection begins just before the tip of the H while ejection from the left ventricle begins after the H tip and may coincide with a flexure sometimes present on the HI segment. This was noted by Reeves[26] and led him to suggest that the first portion of the footward HI segment is produced by right ventricular ejection and that the second portion (after the flexure) is a result of aortic ejection. It should be noted, however, that at the time of the inscription of the HI segment the blood's center of gravity is actually moving footward, not headward. While it may become possible to demonstrate certain specific contributions from the greater and lesser circulations, no convincing evidence of this exists at present.

*The IJ Segment:* The first large mass-displacement of *blood* in systole is headward; it begins at ″I and ends in mid-systole at ″J. This probably reflects (1) the headward displacement of blood from the right ventricle to the pulmonary artery bifurcation and (2) the initial headward displacement of blood into the proximal aortic tree. (3) In addition, headward displacement

* The tips of these waves are not exactly synchronous in our records for reasons given in the appendix. The major displacement wave tips or flexures occur slightly earlier than they should. There is no such phase error in the acceleration waves and their tips give a more precise indication of the time of specific events.

of blood through the inferior vena cava may also make a contribution; Brecher[27] has shown that right atrial inflow is greatly increased during ventricular ejection.

The progressive uptake of blood by the arterial tree distal to the arch finally becomes dominant and the blood's center of gravity reverses direction at ″J; thereafter it moves steadily footward until early diastole.

The factors which govern the duration of the ″I-″J (and I-J) interval are uncertain but they may include arterial distensibility, radius of curvature of the aortic arch, relative length of the aorta proximal and distal to the arch. Diastolic arterial pressure also appears to play a role[16] for if it is increased (e.g., with norepinephrine) the IJ interval is shortened and aortic pulse wave velocity is increased. The reverse occurs when blood pressure is reduced.

Although the curvature of the displacement ″J seems rather smooth there are invisible irregularities which manifest themselves in the region of the acceleration J wave as multiple tips or slurs on the J upstroke and/or downstroke. They often vary systematically during the respiratory cycle.

*The JM Segment:* The largest mass-displacement of the normal human ULF ballistocardiogram, the ″JM, occupies the remainder of systole and is headward, reflecting footward displacement of the blood's mass. During the first two-thirds of the segment the slope is fairly constant although it is usually steepest in its mid-portion. In most normal records this segment shows no particular distinguishing features except for a reduction in slope of the latter one-third. If the change in slope is sufficiently marked (as in Figures 2A and 2C) there may be a synchronous negative acceleration wave, sometimes referred to as K. More commonly, however, after the acceleration J wave the curve descends gradually and irregularly to or below the baseline.

Several investigators[28–30] have suggested methods for estimating stroke volume using certain measurements from the systolic waves of the ULF displacement ballistocardiogram. This approach would seem to hold some promise but the published results thus far are unconvincing.

WAVES INSCRIBED DURING VENTRICULAR DIASTOLE

The displacement waves, ″M and ″N and the acceleration waves, $L_0$, L, M, and N, occur during ventricular diastole.

*The $L_oL$ Segment:* The onset of the 2nd heart sound and the end of the left ventricular systole are coincident in time (see Figure 1). In the acceleration record the small negative wave or flexure, $L_o$, when present is inscribed at or about this same time and is followed by the sharp L wave whose tip is pointed upwards. These two waves have counterparts in the displacement record but they are too small and fast to be visible. Nevertheless they consist in two curvatures; the first (positive, convex upward) should coincide with $L_o$ and the second (negative, convex downward) should be synchronous with L. The explanation for these acceleration and displacement waves is probably to be found in the sequence of events surrounding the closure of the aortic valve. This valve closes as the pressure in the proximal aorta drops rapidly (protodiastolic phase) to reach a minimum value at the nadir of the incisura. This phase is associated with a transient retardation of flow in some parts of the aorta and its branches and actual reversal of flow in others.[23,31,32] The effect should be a sudden, transient reduction in the rate of footward mass-displacement of blood which would be represented by a slight curvature (convex headward) or "shoulder" in the body displacement record and by the $L_o$ event in the acceleration record. The transient reduction of aortic pressure and flow at the time of the incisura is followed by similar transient increase in pressure and flow in the aorta which might be expected to produce a brief augmentation of the footward mass-displacement of blood. This would be represented in the body displacement record as a negative curvature (convex footward) and in the acceleration record as the L wave.

*The LM and MN Segments:* Shortly after the end of right and left ventricular systole the direction of the body's displacement is reversed (at ″M) and during early diastole it moves footward rather rapidly for about 0.10 sec until at ″N the slope changes and becomes flatter. The corresponding changes in the blood's center of gravity (see Figure 7) would

be the termination of its footward movement at ″M, a rather rapid headward movement during early diastole, followed usually by a slower headward movement after ″N. In the normal human acceleration record the L wave is followed by a sharp footward deflection, the LM segment, which terminates in the negative M wave tip synchronous in time with the displacement ″M flexure. The acceleration MN segment coincides with the displacement of ″MN segment.

*Significance of Venous Blood Flow:* The origin of the waves in the ″M-″N and (M-N) region has not been established with certainty and a number of factors may be responsible (for discussion see Honig and Tenney[36,37]). There are several reasons for believing that venous return to the heart may play a part in the origin of these diastolic waves. It will be assumed here, as in the earlier discussion, that the flow of blood through the inferior vena cava considerably exceeds that through the superior vena cava and so venous return therefore constitutes a headward mass-displacement of blood. The ″M-″N interval seems to coincide approximately with the rapid filling phase of ventricular diastole. In humans the end of isometric relaxation (determined by electrokymograms and records from esophageal pressure balloons) and the beginning of ventricular filling occur at or near the time of the ″M and M waves, while rapid filling ends in the vicinity of the ″N and N waves. The rather close temporal relationship between the ″N and N waves and the 3rd heart sound has already been referred to and the latter is known to occur near the end of the rapid filling phase. Finally, in dogs simultaneous ULF acceleration ballistocardiograms and right atrial pressure records have shown that the pressure peak "v" coincides with the tip of the M wave and the subsequent rapid fall in atrial pressure ends at or near the N wave.[16]

The motions of systemic venous blood associated with these events must be considered as the sum of two components. The first, which represents the blood flow from atrium to ventricle, should be small for not only is the distance between them small but the direction of flow is at an angle of approximately 45° from the longitudinal axis. The second component represents headward blood flow through the inferior vena cava to the right atrium and this is known to increase considerably during rapid ventricular filling.[27] Although the "effective" distance traversed by the blood in reaching the atrium is unknown, this component may be the dominant one in the origin of the headward ″MN displacement of blood and the corresponding ″MN and MN events of the human ballistocardiogram.

In deriving the D, V, and A ballistocardiograms Noordergraaf[19,20] took no account of the movement of blood in the veins but considered only arterial uptake and run-off of blood. Nevertheless his summated curves show events which appear to correspond with the ″MN events of the normal displacement ballistocardiogram and its derivatives. Although this would seem to minimize the importance of venous blood flow in the origin of these waves, such is not necessarily the case. At the beginning of diastole there is an excess quantity of blood stored in the arteries of the lower part of the body; its progressive run-off during early diastole shifts the center of gravity of the blood headward. However, the blood which disappears from the lower arterial system during this period may in fact be the same quantity that appears on the venous side and returns to the heart. This matter will require further clarification. In any case, changes in the center of gravity of blood and body after the ″N wave should depend on the relative volumetric rate of run-off from the arteries and return through the veins.

Reeves[26] has called attention to the pair of small waves often present on the MN segment of the acceleration record (see Figures 1 and 3B) and observed that the first (positive) of the two peaks in his records corresponded in time to that given for the end of right ventricular systole by Braunwald. This peak was labeled $L_R$ because he thought it might be associated with the closure of the pulmonary valve and the L wave was labeled $L_L$ because of its apparent relationship to aortic valve closure. Further evidence will be needed to validate these points. Our limited data from dogs indicate that the pulmonary artery incisura occurs before the

L wave[16] rather than after it as the Braunwald data from humans suggest.

It should be again emphasized that what has been said regarding origin of the normal ballistocardiogram represents tentative views based largely on indirect evidence. Any given wave or event in the ballistocardiogram represents the algebraic sum of a number of different circulatory events, some adding, others canceling, which may be taking place concurrently. The validity with which the wave is ascribed to one or more dominant factors will depend on the relative weight assigned to each of the factors operating at the time. At present these are nothing more than crude estimates because it has not been possible to measure them quantitatively in man. The views expressed here therefore constitute only a rough framework which will require modifications and revision as additional information accumulates. Current research in the experimental animal has already begun to yield substantial results and it promises to be an important source of information in the future.


## Summary

(1) The general characteristics of normal human displacement (D), velocity (V), and acceleration (A) ballistocardiograms from an ultra-low frequency (ULF) system have been described.

(2) Detailed time and amplitude measurements were made on the records (D, V, and A) obtained from 100 normal subjects from 20 to 39 years of age and some of the results reported.

(3) The possible role of certain general physical properties of the circulatory system in the origin of the ULF ballistocardiogram was briefly considered.

(4) The temporal relationship of human ULF ballistocardiograms (D, V, and A) to various mechanical events in the cardiac cycle was discussed. Tentative views were expressed concerning the origin of some of the waves of normal ballistocardiograms.

(5) The design, construction and performance of a practical and convenient ULF ballistocardiographic system, based on the differential-pendulum principle, is described in an appendix.


## Appendix


Samuel A. Talbot, ph.d., Joseph H. Condon, William Soper, b.s., *and* William R. Scarborough, m.d.

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### (A) Design and Construction of the Differential Pendulum Ballistocardiograph

The ultra-low frequency ballistocardiographic bed to be described was produced in this laboratory and was one of the early models in a developmental program.* The instrument is shown diagrammatically in Figure 9. The unusual feature of this design is that although the bed is only 25 inches high, its natural frequency ($f_n$) is quite low (0.25 c/s). This is accomplished by supporting a platform on 4 specially designed legs, each of which consists of a simple positive pendulum and a nearly equal negative (or inverted) pendulum. The construction of these legs is shown in Figure 9D. The positive pendulum is above; it is made of wire, and is suspended from the top of the leg. The negative pendulum is below; it is made of dural tubing, and is connected to the frame at the bottom of the leg by means of a frictionless flexural coupling. Joining the two pendula is a short link—at whose midpoint is a flexural hinge supporting the load. The platform is supported on these four legs via two transverse bulkheads, to which the four hinges are bolted. The legs must be accurately vertical.

To a first approximation the natural frequency of such a suspension is independent of the subject's weight, being determined by difference in lengths a and a′ of the positive and negative pendula respectively: $f_n = \frac{1}{2\pi}\sqrt{\frac{g}{a}\left(\frac{a' - a}{a}\right)}$ (e.g. at $f_n = 0.25$ c/s, with $a = 10$ inches, then $a' = 10.62$ inches). The equivalent simple pendulum $\left(f_n = \frac{1}{2\pi}\sqrt{g/a}\right)$ would be 13 ft long, and plagued by vibrations in the wires. However, stability of this suspension depends on non-rotary hinges: this introduces some springiness, and so a small weight-dependence of frequency. Also, with these pendular legs, the level of suspension is well below the c.g. of the body, giving the bed a strong moment in roll; this does not yield a design for good lateral response. (Another design without these limitations, has been devised for

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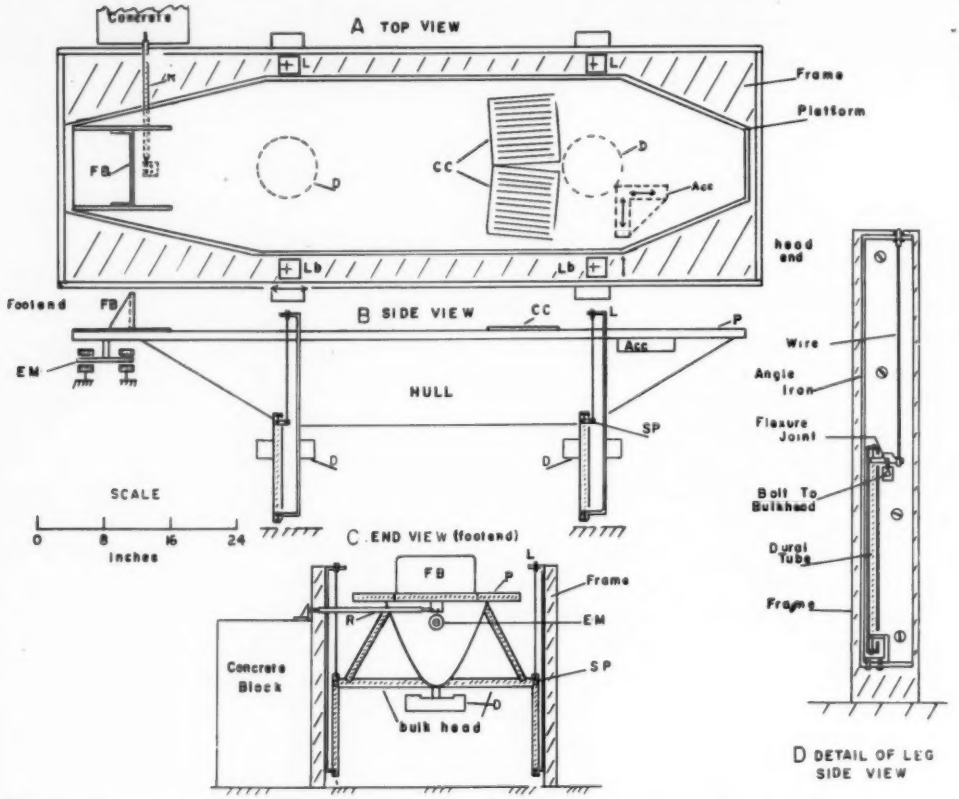


Fig. 9. Diagrams of the construction of the differential-pendulum ULF bed. Portions of the wooden frame are indicated in A, C, and D but are not included in B for reasons of clarity. Symbols: L: differential-pendulum leg; $L_b$: legs used for balancing platform; R: restraint rod to prevent lateral motion; FB: footboard; Acc: accelerometers; P: platform; EM: electromagnetic transducer; SP: suspension point for platform; D: dampers; CC: rubber pads with grooves for seating the postero-lateral chest constraints.

3D BCG beds, where an unconstrained lateral record is required.)

The platform which supports the subject was made of aircraft honeycomb or Aircomb†; it is 1 inch thick, 81 inches long and 20 inches wide. The moving platform is surrounded by a rather rigid outer wooden frame from which the four legs are suspended. The platform is locked to this frame when the bed is not in use. In order to avoid spurious mechanical artifacts arising in the platform itself, every effort was made to insure its flexural rigidity. Toward this end a hollow dural "hull," much like that of a boat, was applied to the lower surface of the platform. A variable speed mechanical "shaker" used to drive the platform made it possible to identify the sources of spurious platform vibration, and these were subsequently eliminated.

The nature of this suspension permits the platform to move from side-to-side (laterally) as well as from head-to-foot (longitudinally). A light restraint rod (R) coupled by shim stock to the foot end of the platform and to one side of the frame eliminates lateral motion at this end but allows free movement at the head end. This coupling imposes no restriction on motion in the longitudinal axis and produces no significant interaxial transfer. The natural frequency in the lateral mode is comparable to that in the longitudinal, namely 0.25 c/s.

Two viscous dampers were added, one near the head end and one near the foot end of the bed, and these permit damping to be adjusted independently in the two modes. The dampers consist in cylindrical containers of silicone and thin metal discs attached by light dural rods to the platform in such a way that the depth of the discs in the silicone may be adjusted. The degree of damping chosen for both head-foot and lateral was 25 per cent of critical (damping ratio = 0.25) with a 150-lb mass on the platform. At any given setting of the damper, the damping produced should depend on the mass on the platform, decreasing as the mass is increased. However, with this bed there is a certain amount of stretch or "give" in the supporting legs so that with heavy persons the damping discs are somewhat deeper in the silicone and with light persons they are shallower. The result is an almost complete automatic compensation for differing body weights. This con-

† Douglas Aircraft Co.

sideration and the fact that the exact degree of damping used is not a critical matter makes it possible to use the same setting for all persons regardless of weight. The degree of damping used represents a compromise; it is large enough to provide stability and minimize baseline weave in acceleration records during normal respiration but is sufficiently low as to minimize errors in phase at low frequencies. (For over-all performance of the system, see below.)

The upper surface of the platform is covered with a light thin rubber padding with a pebbled surface to prevent slipping of the body on the surface. Coupling between body and platform is improved by use of a footboard, adjustable in position, and a pair of postero-lateral chest constraint blocks. The latter slip into either side of the chest and are curved to fit the contour of the postero-lateral chest extending from the region of the mid axillary line to a point partially beneath the back. Corrugated rubber pads with longitudinal grooves were glued to the bottom of each block and to the surface of the platform. These constraints are easy to fit to chests of varying size and once pushed in against the chest, the opposing rubber grooves engage and the blocks are, in a sense, locked into place.*

All electrical connections between the platform and the supporting frame were made with very light, flexible wire which was led off to the frame by way of the lateral restraint rod. Such precautions were necessary to avoid additional, and usually alinear, external restoring forces.

In order to correct any platform imbalance which may result from differences in distribution of body mass from one person to the next, a balancing mechanism was incorporated. This made it possible to tilt the upper end of one of the legs in the head-foot direction and that of another leg in the side-to-side direction so as to allow balancing in both directions. The bed is properly balanced when a position indicator on the bed is aligned with a reference on the frame.

The total weight of the platform including that of the various devices attached to it (transducers, dampers, constraints, footboard, etc.) is approximately 15.0 lb (6.8 kg).

## (B) Transducers and Associated Electronic Equipment

### (1) Accelerometers

Two accelerometers are mounted on the under surface of the platform near the head end of the bed; one is oriented in the head-foot axis, and the other in the lateral axis. These accelerometers are of the self-generating, seismic reference type based on a modification of a design by von Wittern,† and were fabricated here. The sensing elements used were phonograph crystals to each of which a small mass was attached by means of a short rod. The natural frequency of these accelerometers is approximately 70 c/s. Silicone was introduced between the mass and case to provide damping; the damping ratio chosen was 0.7 (70 per cent of critical). Special preamplifiers were built for the accelerometers and these include Miller circuits to extend the low frequency response; the resulting "corner frequency," $f_c$, is sufficiently low (about 0.13 c/s) as to insure that no significant errors are introduced at low frequencies. The preamplifier outputs are fed into cathode followers which drive Hathaway oscillographic galvanometers (natural frequencies of about 100 c/s). Over the BCG band of 1-35 c/s over-all amplitude response is essentially flat (less than 10 per cent error) and the phase response is such that there is a small constant time delay (0.009 sec) at high frequencies. However, the presence of a considerable amount of floor noise in the lateral records (but not so evident in the head-foot) made it necessary to use a high-cut electronic filter ($f_c$ at 40 c/s) with the lateral accelerometer equipment; at 30 c/s the amplitude loss is 30 per cent and there is a small constant time delay (0.013 sec).

### (2) Velocity and Displacement Transducers

The head-foot velocity and displacement records are derived from the output signal from a coil-magnet pick-up.* An Alnico magnet $^3/_4$ inch in diameter and $4^3/_4$ inches long is fastened at its center to the foot end of the platform (see EM in Figure 9). Centered around either end of the magnet is a coil of 40,000 turns and these are rigidly fixed to a concrete block on the floor. The output of these coils is fed through a high-cut filter of the L-C type with a corner frequency of 52 c/s; at 30 c/s amplitude loss is 30 per cent and there is a small constant time delay (0.006 sec). The filter output is fed through a resistance divider for the velocity record and through an integrator for the displacement record. The corner frequency of the integrator, originally thought to be quite low (0.06 c/s) was recently found to be much higher (0.33 c/s) as a result of an impedance mismatch. At 1 c/s amplitude is down 10 per cent and there is a phase lead of 18°; these errors become progressively smaller at higher frequencies. The displacement and velocity signals are fed into d.c. amplifiers which drive oscillographic galvanometers ($f_n$ of 100 c/s).

### (3) Recorder

Records are obtained with a 6-channel Hathaway oscillographic recorder. A 750 c/s galvanometer is used for heart sounds; the other five galvanometers have natural frequencies of about 100 c/s.

## (C) Calibrations

The bed and the transducers were calibrated mechanically by applying motions of known magnitude

* We are indebted to Dr. William Dock for this useful idea.

† Personal communication; unpublished data.

* A number of these components were obtained through the courtesy of Mr. Maurice Rappaport of the Sanborn Co.

to the platform. Then each transducer and its amplifier were calibrated electrically so that a standard input signal is proportional to a known platform motion. The accelerometers are calibrated by switching one end of a capacitor by 1.34 volts, the other end of the capacitor being connected to the signal input lead; this change in input signal is equivalent to 2.14 milli-G. The velocity and displacement equipment is calibrated by inserting a small potential in series with the input to the amplifier, a method similar to that for ECG calibration or standardization; these signals are proportional to a displacement of 64 $\mu$ and a velocity of 1.7 mm/sec. All four calibrations are made during each patient study.

### (D) Over-all Frequency Response Characteristics of Ballistocardiograph Bed, Transducers and Associated Equipment

The bed loaded with dead weight was driven with a mechanical shaker over a frequency range of 0.5–35 c/s in order to test the over-all frequency response characteristics of the bed, transducers and associated electrical equipment. The responses were flat to 35 c/s except for those transducers described above with which high-cut filters were purposely used to reduce their responses to high frequency events. The frequency range over which it is desirable to obtain a flat response with minimal phase error depends on the frequency content of the motions being measured. The acceleration record contains more high frequency detail and their faithful reproduction requires a more extended range than is necessary for velocity and displacement records. The lower limit of frequency response is determined by the low frequency content of the displacement record. This usually is taken to be 1 c/s, the fundamental frequency of the heart beat, and is probably a conservatively low figure. Dynamic tests with the equipment revealed that low frequency response is limited only by the low frequency cut-off (at 0.25 c/s) of the bed itself. Above 1 c/s, this results in less than 10 per cent amplitude error and less than 18° (0.05 sec) in phase lead. The integrators used in recording displacement tend to decrease the amplitude error but to increase the phase lead at low frequencies.

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# Estimation of Stroke Volume by Means of the Ballistocardiograph*

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THE USE of the ballistocardiograph as a means of determining cardiac output was the earliest aim in ballistocardiography. There have been two determined attacks on this problem, one by Starr and his co-workers[1] in 1939 using the high-frequency ballistocardiograph and the other by Nickerson and his associates[2] in 1947 using the low-frequency, critically damped instrument. These two groups of investigators devised equations of an empirical type to predict the stroke volume from the dimensions of the ballistic pattern and demonstrated a degree of correlation between the values so determined and those given experimentally by other methods such as by a modified Grollman gas method or by the direct Fick method with atrial catheterization. The results of these workers have been critically reviewed by Taylor and Tiede[3] and the work of Nickerson especially by Cathcart and co-workers.[4]

Other workers have arbitrarily chosen various dimensions from the ballistic pattern and used these measurements as indices of stroke volume without, however, correlating their data with independent methods. Recently, Haas[5] has presented a theoretic discussion of a method of computing the stroke volume for the ultra low-frequency system.

The present paper reviews the simplest theory underlying the application of the ballistocardiograph to the measurement of cardiac output and demonstrates an attempt to change the method from an empirical, dependent method to one that is independent of calibration by some other method.

## METHOD

The basic problem of the determination of the stroke volume from the ballistic pattern can be stated[6] in terms of the equation of conservation of momentum, namely:

$$M_B V_B = m_R v_R + m_L v_L \qquad \text{(I)}$$

where $M_B$, $m_R$, and $m_L$ are the mass of the body-ballistic system and of the blood ejected from the right and left sides of the heart, respectively, and $V_B$, $v_R$, and $v_L$ are the corresponding mean velocities at ejection.

The quantity $M_B$ is known and the quantity $V_B$ can be determined from the ballistic pattern. In the work of Nickerson[6] an equation of motion for a low frequency, critically damped ballistic system was set up and from this equation it was possible to show that the momentum of the ballistic system as a function of its mass and velocity was determinable from the ballistocardiogram. Specifically one measures the distance ($D$) moved by the bed in passing from the I-trough to the J-peak and one also measures the time ($T_2$) required for this movement. The resulting formula is

$$M_B V_B = \frac{gF}{4\pi^2 n_0^2 T_2 R} = \frac{11.03F}{T_2 R} \qquad \text{(II)}$$

where $F$ is the grams of force required to move the ballistic system through the distance ($D$) and $R$ is given by the formula

$$R = \left[e^{-aT_2}\right]\left[C - e^{-aT_1} - \left(\frac{T_1}{T_2}\right)\frac{(e^{-aT_1})}{(e^{-aT_2})}\ (e^{-aT_1} - 1)\right] \qquad \text{(III)}$$

* From the Chicago Medical School, Department of Physiology and Pharmacology, Chicago. This investigation was supported by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service.

in which $T_1$ is the time interval from the H-peak to the I-trough and a $= 2\pi n_0$, where $n_0$ is 1.5 cycles per second and $C = 1.37$.*

Having evaluated $M_B V_B$ there remain four quantities to be considered. For the normal heart it is assumed that $m_L = m_R = m$ and $v_R = v_L = v$ so that the general equation (I) reduces to the form

$$2mv = 2Sdv = M_B V_B \qquad \text{(IV)}$$

where $d$ is the density of blood and is assumed to be 1.055, $S$ the stroke volume of blood ejected into the aorta, and $v$ its mean velocity of ejection.

In the empirical formula used by Nickerson[2] there was no attempt to estimate $v$. It was merely assumed that $v$ was an inverse function of the average blood pressure opposing the ejection of blood. At the time the basic formulae were devised[6] Nickerson published also a formula in which $v$ was estimated from the time interval between certain events in the ballistic pattern and from the distance between certain points in the aortic tree believed to be involved in succession in these events.

In the present work the time interval selected is from the beginning of the headward ejection to the beginning of the footward thrust from J to K. This time interval is given by

$$T = T_{HJ} + 0.02 \text{ second} \qquad \text{(V)}$$

where $T_{HJ}$ is the interval between the H-peak and the J-peak (or the beginning of the increased rate of descent along the J K limb), and the two hundredths of a second represents the interval between the beginning of ejection and the appearance of the peak of the H-wave.[7] The distance travelled by the blood during this time $T$ is from the beginning of the ascending aorta to some point well down the descending aorta. This point is approximately half way from the aortic valve to the iliac bifurcation so that the distance is approximately $^1/_{10}$ of height of subject. Hence the maximum velocity is H/10 $T$ and the mean velocity is one-half of this assuming a parabolic ejection front so that

$$v = H/20\ T \text{ cm/sec} \qquad \text{(VI)}$$

* $C = 1.50 - x/2$ where x is the fraction (about $^1/_4$) of the blood moving headword from the aorta.[6]

The formula for stroke volume becomes therefore from equations II, III, IV, V, and VI

$$S = \frac{105\ FT}{RHT_2} \text{ cc} \qquad \text{(VII)}$$

## Clinical Application

This formula was applied to data on five subjects on whom direct Fick cardiac output measurements were made in connection with an earlier project.[2] The results are shown in Table I and Figure 1.

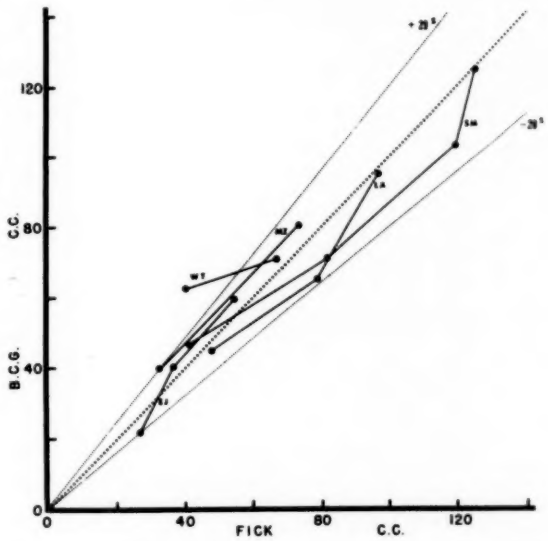


Fig. 1. Correlation between stroke volumes measured by the Fick method and volumes computed from BCG (see formula VII).

Inspection of Table I shows that the agreement between the stroke volumes measured by the Fick method and the volumes ($^S$VII) computed from formula (VII) are not only of the same order of magnitude but are in surprisingly good agreement. This encourages further investigation.

There is an observed trend of variation with average pressure in these results. This is most probably a function of the elasticity of the large vessels. Correction of these values by dividing $^S$VII by $K$ where

$$K = 2.00 - .0094P$$

produces the results in column $^S$VIII which are in good agreement with the Fick results. The correction above suggests that at values of pressure approaching zero the effective length of the

TABLE I
Stroke Volumes in Milliliters

| Subject | Age | Pa | $^{S}$Fick | $^{S}$VII | K | $^{S}$VIII |
|---|---|---|---|---|---|---|
| LA | 15 | 74 | 47.7 | 58.2 | 1.30 | 44.7 |
| LA | 15 | 84 | 78.4 | 78.2 | 1.21 | 64.6 |
| LA | 15 | 95 | 96.3 | 105.0 | 1.11 | 94.6 |
| EJ | 30 | 81 | 26.7 | 26.8 | 1.24 | 21.6 |
| EJ | 30 | 85 | 36.5 | 48.0 | 1.20 | 40.0 |
| EJ | 30 | 89 | 54.0 | 68.6 | 1.16 | 59.1 |
| SM | 39 | 66 | 41.0 | 63.6 | 1.38 | 46.2 |
| SM | 39 | 71 | 81.3 | 93.8 | 1.33 | 70.5 |
| SM | 39 | 76 | 119.0 | 132.2 | 1.29 | 102.4 |
| SM | 39 | 76 | 125.0 | 160.0 | 1.29 | 124.0 |
| WT | 52 | 57 | 40.1 | 91.5 | 1.47 | 62.3 |
| WT | 52 | 93 | 66.1 | 79.2 | 1.13 | 70.1 |
| MZ | 22 | 67 | 32.1 | 53.8 | 1.37 | 39.3 |
| MZ | 22 | 103 | 73.0 | 82.2 | 1.03 | 79.8 |

aorta approaches the full length, H/5, instead of the average H/10 assumed previously. Similarly, as the average pressure rises above 100 mm the effective aortic length decreases below H/10. This linear correction formula is in agreement over part of the range with an exponential function $K=2e(-P/157)$ which is probably a more exact representation of the variation of the effective length with pressure and elasticity.

## Conclusions

In conclusion, it may be said that this excursion into more quantitative ballistocardiography points up some interesting speculations on the possibility that ballistocardiography may provide an independent method for the estimation of stroke volume in the normal subject. It also answers some of the criticism of empiricism directed against the earlier ballistic stroke volume formula and perhaps draws attention to some limitation of accuracy in the Fick method—especially evident on serial observations on the same subject.

This investigation furthermore lays the groundwork for our investigation of the measurement of the output in the abnormal heart by indicating at which point approximations have been introduced in order to simplify the problem for the normal heart.

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# Acute Pericarditis with Friction Rubs

A. A. Luisada, M.D. *and* J. Szatkowski, M.D.

Chicago, Illinois

This 35-year-old white female was admitted to the hospital because of fever and chills of 10 days' duration, left upper chest pain increasing during inspiration, cough, and sneezing of about three to four weeks' duration. Four days prior to this hospital admission, she was placed on a "broad spectrum" antibiotic, with no apparent improvement.

PHYSICAL EXAMINATION

There was slight dyspnea at rest but no cyanosis or neck vein engorgement. B.P. was 120/75; pulse 100, regular. The *lungs* were clear to percussion and auscultation. The *liver* was palpated 2–4 cm below the left costal border.

*Heart:* Apical impulse was in the 5th intercostal space, 2 cm outside the mid-clavicular line. There were no thrills. High-pitched, systolic and diastolic murmurs, giving the impression of being very close to the ear, were heard over the entire precordium, loudest over the 4th right interspace and upper part of the sternum (friction rubs?). $M_1$ loud, $P_2$ louder than $A_2$.

The *chest x-ray* showed enlargement of the left atrium and ventricle.

PHONOCARDIOGRAM

In order to clarify the diagnosis, a phonocardiogram was recorded. This showed (Fig. 1) two groups of high-pitched vibrations, one in presystole, one in mid-systole. The presystolic group was terminated abruptly and was widely separated from the 1st sound. These were considered typical "friction rubs."

HOSPITAL COURSE

The patient was put on Meticorten and Terramycin. A steady, gradual improvement was noted. The temperature became normal and the intensity of the "rubs" decreased. On the 7th hospital day, they were hardly audible and the patient was discharged on the 12th hospital day.

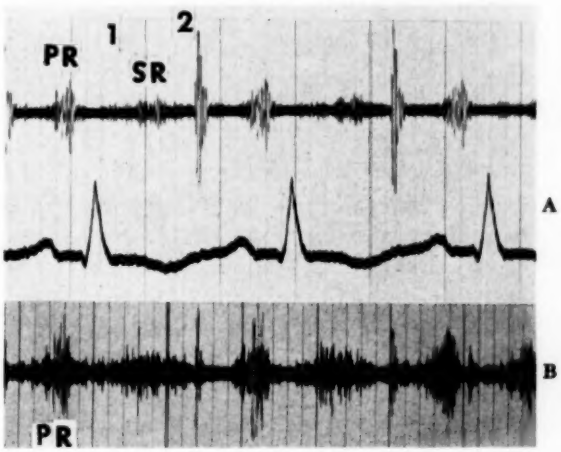


Fig. 1. (A) Phonocardiogram above and ECG (below). (B) Filtered phono (range 120–240). Both tracings reveal a pre-systolic rub (PR) and a systolic rub (SR). The two tracings are exactly superimposed; however, on account of slight difference of rate, the 2nd and 3rd complex of the lower tracing anticipate slightly in comparison with those of the upper tracing.

Readers are invited to submit reports of interesting cases and illustrative tracings for this department. These should not exceed 1,000 words in length. Although not necessarily original, all material submitted should have teaching value.

# Letters to the Editor

## Anticoagulants in Myocardial Infarction

Dear Sir:

The provocative article of Rosenberg and Malach, Acute Myocardial Infarction in a City Hospital. II. Experience with Anticoagulants, Am. J. Cardiol. 2:71 (July) 1958, should not be enshrined into the medical literature without some critical comment when it purports demonstration of the lack of effect of anticoagulant therapy for myocardial infarction, albeit in an indigent population. I believe that the reinterpretation of the authors' own data should lead one to an entirely different conclusion.

The over-all mortality rate of almost every other case is reminiscent of a past age in cardiology for these United States so that the factors which may have been responsible must likewise have destroyed those among the anticoagulant treated group as well as the so-called control or untreated group. The treated patient is certainly not shown in a favorable light when he succumbs to factors unrelated to the therapy. One can be sympathetic with the problems of lack of private nursing care and the other problems of the charity hospital and recognize that they do affect mortality but one must be cautious before accepting results obtained under these circumstances which cannot help but reflect the greater weakness of the system than the other links in the therapeutic chain, particularly the anticoagulant therapy which a portion of the patients happened to receive.

Even if one generously excludes the influence of the unusually high over-all mortality rate, analysis of the remaining data supports the beneficial effect of anticoagulants in this reported series. On page 75, the authors state, "We feel the ineffectiveness of the anticoagulants in our patients is even more meaningful when one considers that over twice as many 'poor risk' cases (28 per cent) received the drugs as 'good risk' cases (13 per cent). Any favorable influence of the anticlotting agents should be demonstrable in the 'poor risk' group." By the authors' own admission, therefore, the untreated group cannot be considered a control group in any sense because it represents a selection of cases with a better outlook than the group subjected to therapy which had a higher incidence of "poor risk" cases. By achieving the same mortality in the group with the poorer prognosis, one has achieved a salutary effect. One can concur with the authors that the tabulation of the breakdown into good and poor risk cases in Table IV "in each of the subcategories is too small for valid appraisal." One cannot help being struck by the significantly greater mortality among "good risk" cases in the treated than in the untreated group and one wonders how this came about. Were it not for these inexplicable data, one might anticipate the entire tabulation to be different.

So long as a controversy about the value of anticoagulant therapy continues, good clinical studies will be worthwhile; but they must fulfill acceptable experimental design, expert anticoagulant therapy, and impartial analysis. Lesser efforts cannot improve present position.

William H. Wehrmacher, M.D., F.A.C.C.
Chicago, Illinois

### Authors' Reply

Dear Sir:

In reply to the remarks of Dr. William H. Wehrmacher concerning our experience with anticoagulants, one must say that the controversy over the use of these drugs will continue far into the future. The paper under discussion was in no way designed as an experimental study but merely reports our observations of a group of 264 patients with acute myocardial infarction in one year at the Kings County Hospital. Well-designed experimental studies have already been done many times, principally by Wright and his colleagues, and have presumably demonstrated

the value of anticoagulants in this disease. It is for this reason that in our report the group not receiving these drugs was labeled as "untreated" rather than "control."

There would appear to be general agreement that the anticoagulants cannot be expected to favorably influence mortality in the first 48 hours, certainly not a slow-acting agent such as Dicumarol, which was the drug employed in 57 of our 66 treated patients. Likewise, most workers attest to their value at least in so-called "poor risk" cases (employing the criteria of Zohman). Therefore, the effectiveness of anticoagulants should be easily demonstrable in the post-48 hour mortality of the "poor risk" group. In our series, such an effect was not observed. After a careful analysis we concluded that such factors characteristic of a city hospital population as older age, low socio-economic status, absence of pre-hospital medical supervision and lack of private nursing care in the hospital may counterbalance and indeed outweigh any theoretic advantage of the anticoagulants. At least, this was true in our series of cases observed during a period of one year.

Regarding the "good risk" cases, the observed adverse effect of the anticoagulants upon mortality is not significant because of the small number of patients (8 treated versus 52 untreated). Actually, in view of the aforementioned characteristics of a city hospital population, these "good risk" cases, although satisfying the criteria of Zohman, are not comparable to those in other series emanating from non-municipal institutions. Indeed, perhaps the factors of advanced age, lack of pre-hospitalization medical supervision, low socio-economic status and absence of private nursing care should be added to the criteria for "poor risk" cases.

To further substantiate our conclusions we are currently enlarging our review to encompass a period of five years at the Kings County Hospital. At the same time, we are comparing our series already reported with those of two other voluntary hospitals associated with the State University Downstate Medical Center. Preliminary impressions would seem to bear out what has already been stated, but we must wait for all the data to be compiled.

In the meantime, one must concede the effectiveness of the anticoagulants in acute myocardial infarction, certainly in many "poor risk" cases. At the same time, one must recognize that other factors, as described above, may outweigh any beneficial advantage these drugs may possess. Indeed, the controversy as to their effectiveness will continue.

BENJAMIN A. ROSENBERG, M.D.
MONTE MALACH, M.D.
Brooklyn, New York

# Progress Notes in Cardiology

*Edited by* EMANUEL GOLDBERGER, M.D., F.A.C.C.

New York. New York

Investigators and research workers are invited to submit, with a view to publication in an early issue, résumés of work in progress or recently completed.

## Significance of the Superior Vena Caval Syndrome

Obstruction of the superior vena cava is seen with increasing frequency. Dr. William J. Bruckner (VA Hospital, Pittsburgh) investigated a series of cases covering the last ten years, and compared them with reports published previously (*A.M.A. Arch. Int. Med.* 102: 89, 1958). In comparison with previous findings, he noted that obstruction of the superior vena cava is now the result of malignancy in more than three-quarters of all cases. The malignancy is nearly always bronchogenic carcinoma. (Aortic aneurysm, or traction, or compression by scar tissue due to chronic mediastinitis caused the syndrome in less than 10 per cent of the patients.) Whenever superior vena caval obstruction had existed for six months or longer, the etiology was benign. The importance of this finding lies in the presumed curative procedure available through surgical by-pass.

The diagnosis of superior vena caval obstruction is difficult. However, the early use of venography, venous pressure determinations, and infrared photography are helpful in determining which patients are still operable.

## The Etiology and Pathogenesis of Rheumatic Fever

In recent years, the relationship of rheumatic fever to infection with group A streptococci has been demonstrated in many ways. Swift believed that rheumatic fever was related to successive infections with different serologic types of group A streptococci. Many investigators believe that rheumatic fever represents a state of hypersensitivity (allergy), possibly to one or more streptococcal antigens. The nature of the streptococcal antigen or antigens responsible for the development of the hypersensitivity state has been unknown up to now. Others believe that autoantibodies or antitissue antibodies against heart muscle are responsible for the lesions of rheumatic fever.

In a paper just published (GOLDBERGER, E.: *Acta med. scandinav.* 161: 347, 1958) we have described a new concept for the etiology and pathogenesis of rheumatic fever. We believe that rheumatic fever occurs as a result of two simultaneous processes: (1) a reinfection with a group A streptococcus of the same serologic type which previously had caused infection; and (2) a specific antigen-antibody reaction, similar to but not identical with that of serum sickness, which results from the reliberation of type-specific streptococcal M protein into the systemic circulation.

On the basis of this concept, prevention of rheumatic fever becomes a problem of preventing group A streptococcal reinfection. Prophylaxis with penicillin is effective in most patients. However, we have suggested that groups of patients with a history of rheumatic fever should not be hospitalized or confined together, if possible, because the rheumatic fever represents a reinvasive type of communicable disease. In other words, a patient can not only spread a streptococcal reinfection to other members of the

group and so cause a reactivation of rheumatic fever, but can also be similarly reinfected and similarly develop a reactivation of rheumatic fever from any other member of the group.

Host factors are also important, because streptococci may remain viable for years in tonsils, for example, even though no overt signs of streptococcal infection are present. However, when the resistance of the patient becomes lowered, these streptococci may cause a reinfection and can then precipitate an attack of rheumatic fever.

Once rheumatic fever develops, the main object of therapy, according to the concepts presented in this paper, should be the elimination of group A streptococci from the body of the patient, in order to convert rheumatic fever into a self-limited disease like serum sickness. Theoretically, penicillin is the drug of choice. However, in the doses which are ordinarily used, it is apparently not able to kill streptococci, otherwise sensitive, which are in a state of low-grade metabolic activity. Methods of overcoming this difficulty, such as the concomitant use of streptomycin, or the concomitant use of cortisone or its derivatives, to reactivate metabolically the streptococci are discussed in the paper. Our belief at the present time is that rheumatic fever should be treated with doses of penicillin similar to those used for subacute bacterial endocarditis.

## *Did you know that . . .*

The most important criterion for mitral valve surgery in a patient with mitral stenosis is the presence of pulmonary hypertension. This can usually be determined by the presence of the following symptoms and signs:

(1) Hemoptysis and nocturnal dyspnea. However, these symptoms can occur in patients who have only mild or moderate pulmonary hypertension and are not of much value in determining the degree of pulmonary hypertension.

(2) Prominent auricular venous waves in the neck veins; this is an important clinical sign of pulmonary hypertension in patients who have sinus rhythm.

(3) A forceful systolic pulsation to the left of the sternum at about the level of the fourth intercostal space; this is also a good sign of both right ventricular hypertrophy and pulmonary hypertension.

(4) A palpable 2nd heart sound is a good sign of moderate or severe pulmonary hypertension.

(5) A loud and split 2nd heart sound is not a reliable sign of marked pulmonary hypertension, because it may occur in the early stages of pulmonary hypertension.

(6) A Graham Steell murmur, however, is a good sign of pulmonary hypertension. The murmur of aortic insufficiency should not be mistaken for a Graham Steell murmur.

(7) Electrocardiographic evidence of right ventricular hypertrophy, such as a tall R in lead $V_1$ is also evidence of pulmonary hypertension.

(8) Fluoroscopic and x-ray examination will reveal increased or marked prominence of the pulmonary arteries with marked pulmonary artery pulsations.

The shape of the pulmonary artery and its branches is related to the severity of the pulmonary hypertension. When the pulmonary artery pressure is less than 40 mm Hg, the pulmonary artery and its branches may appear normal on the x-ray film. When pulmonary hypertension is present and the pulmonary artery pressure is between 40 to 70 mm Hg, the main branches of the pulmonary artery are enlarged and the distal branches are narrow, irregular and tortuous, especially in the lung bases close to the heart. When the pulmonary artery pressure exceeds 70 mm Hg, these changes are widespread. E. G.

# Cardiac Resuscitation

*Edited by* PALUEL J. FLAGG, M.D., F.A.C.C.*

New York, New York

# Long Range Indoctrination

LONG range indoctrination implies an early beginning directed to the first year medical student. Here the basic sciences, anatomy, physiology, physics, chemistry, pharmacology, pneumatology, etc. provide an introduction. The later clinical years offer endless opportunities for the recognition of hypoxic hazards common to every specialty.

With a view to attempting to find out the views of the medical schools on the problem, Dr. George Packer Berry was approached in 1952. Dr. Berry pointed out that the best way to learn the thinking of the Deans on the subject was to attend the annual meeting of the Association of American Medical Colleges to be held at Colorado Springs that fall. While it is not the policy of the Association to allow scientific exhibits at its annual meetings, a display of the causes and the treatment of hypoxia was permitted. The response was most gratifying. Some 25 medical schools expressed a desire to know more about the subject. The following year a more extensive exhibit was presented at the Atlantic City meeting. In the fall of 1954, the Association met at French Lick Springs. At this meeting a direct appeal was made to the Deans in a "blowup" carrying the following:

*Clinical hypoxia is an administrative problem.* Only the Dean has the freedom, the vision, and the drive and can direct the "know-how" to professional asphyxia consciousness.

*Clinical hypoxia is not to be confused with a specific disease or a specific accident.* It cuts across the entire field of medicine.

*Clinical hypoxia cannot be departmentalized.* To attempt to contain it within the limits of a specialty is to overlook asphyxial accidents in others.

### DEPARTMENTAL REFERENCES TO CLINICAL HYPOXIA

The heads of the basic science and clinical divisions were appealed to as follows:

Departmental heads are invited to inspect the 20 departmental references to clinical hypoxia noted below. No order, sequence, or interdepartmental relationship appears. Is not this the position of clinical hypoxia in the medical school as of today?

Viewing the basic sciences, hypoxia could be stressed in departments 1–8; in clinical practice, in 9–20:

(*1*) *Anatomy:* Orientation and relationship of structures in infant and adult with special reference to the cardiovascular, respiratory, and nervous systems; emphasis upon the respiratory system in its relation to anoxic and stagnant hypoxia; location of easily accessible blood vessels for transfusion and intravenous medication.

(*2*) *Physiology:* Integrated function of muscle tone and reflexes; orderly sequence of timing as it affects oxygen saturation in the cardiovascular, respiratory, and nervous systems.

(*3*) *Pathology:* The effects of disintegrated function; gross and microscopic effects of acute and chronic hypoxia; postmortem findings in submersion, carbon monoxide and drug poisoning.

(*4*) *Pharmacology:* Pharmacology of anemic, anoxic, and histotoxic hypoxia from sedatives, analgesics, anesthetics, and curare-like drugs. Reversibility, detoxification, antidotes, allergic reactions.

* President, National Resuscitation Society.

(5) *Chemistry:* Blood and tissue studies with special reference to $O_2$, $CO_2$, and pH in acute and chronic hypoxia; acidotic and non-acidotic acarbia.

(6) *Biochemistry:* Anemic, anoxic, and histotoxic hypoxia in the capillary bed.

(7) *Physics:* Nature, behavior, and management of gases used for anesthesia, resuscitation, and inhalation therapy (pneumatology).

(8) *Radiology:* Diagnosis of cardiovascular and respiratory pathology with special reference to lesions of the airway and pulmonary alveolar bed.

(9) *Medicine:* Pathologic physiology of hypoxia in clinical diseases; danger of overemphasis of cardiovascular at the expense of respiratory stimulation; positioning and airway control of the unconscious patient; clinical appraisal of hypoxic risks.

(10) *Surgery:* Effect of mechanical interference with the pathologic physiology of the cardiovascular and respiratory systems; thoracic and cardiac surgery; thorocoplasty, lobectomy, pneumonectomy, mediastinal shift; myocardial sensitivity to hypoxia and shock.

(11) *Anesthesiology:* Obligation to make generally available the instrumental technical "know-how" for the prevention and treatment of spastic and flaccid asphyxia; acquaintance with pathologic physiology of controllable unconsciousness.

(12) *Obstetrics:* Infant and maternal hypoxia; neonatal hypoxia: antepartum, at delivery and postpartum. Cesarean hazards to mother and child.

(13) *Neurology:* Cell and neuron damage; cerebral palsy and crippling of children; the human vegetable; recovery from protracted and profound hypoxia.

(14) *Pediatrics:* Asphyxia neonatorum; late effects of hypoxia in cerebral palsy, crippling of children; hypoxia accidents in infancy.

(15) *Eye, Ear, Nose, and Throat:* Hypoxic accidents in ophthalmologic surgery under local anesthesia; anoxic and anemic hypoxia in throat surgery under local and general anesthesia; sedation and hemorrhage.

(16) *Medical Jurisprudence:* Legal aspects of hypoxic accidents: Carbon monoxide, submersion, suffocation, hanging, electrocution; diagnosis of somatic death.

(17) *Army:* Battle hazards; extramural accidents as in civilian life, toxic gases; perforating wounds of the chest; cranial injuries.

(18) *Navy:* High atmospheric pressure problems; compression and decompression; submarine problems; air conditioning; carbon monoxide; tolerance; submersion.

(19) *Air Force:* Low pressure problems; hypoxia in high altitude; acceleration and deceleration; CO and $CO_2$ hazards.

(20) *Public Health:* Extramural hypoxia accidents: carbon monoxide, submersion, electrocution, foreign body obstruction.

## Present Status of Problem

It was observed that following the initial introduction in Colorado Springs, interest had waned. It appeared that the Deans, having discussed the problem with their departments of anesthesiology, were assured that the matter was well understood and that it was receiving suitable attention. Unfortunately, this attention was apparently restricted to anesthetic personnel, as shown by requests for instruction from residents of departments of obstetrics, pediatrics, etc., in institutions in which adequate instruction was assured. These requests were received regularly by the National Resuscitation Society which undertook to supply instruction to these applicants without charge. It is not at all unlikely, and quite natural, that suggestions for improvement were resented by departments of anesthesia and that explanations, accepted by the administration without confirmation, left the problem just where it began.

The impasse faced by hypoxia in the medical school, therefore, seemed to turn on two major difficulties; (1) A lack of understanding of the immensity and the urgency of the problem by administrative authority; (2) relegating and leaving the issue in the hands of an intramural specialty (anesthesia), already overburdened by routines and apparently out of sympathy with the broad issues involved.

However, these were not the only difficulties. In a conversation with the Executive Secretary

of the Association of American Medical Colleges in December, 1952, it was pointed out that the medical school curriculum was already saturated and that severe competition was to be anticipated by any new project asking consideration.

What then was the solution which would place this most important problem before the entire student body, which would bypass the apathy and resentment of departmental control, which would not require a definite place in the curriculum and which could meet competition? The answer was a first class, professional, color, sound film to run 20 minutes and which would cost about $20,000 to produce. It was assumed that Industry would be glad to subsidize such a film. A script outline was promptly set up. It was submitted for the consideration of more than 50 industrial corporations. While interest was expressed, no action was taken. At the same time, the outline was sent to the specialty sections of the A.M.A. for their considered approval. Of the ten sections queried six specifically approved, four abstained.

A request for assistance was then made to the U. S. Public Health Service through Surgeon General Scheele. Dr. Bartholomew Hogan, Surgeon General of the Navy, expressed his interest in cooperation by designating Capt. Robert V. Schultz, Head of the Audiovisual Department of the Navy, to act as technical advisor if and when the film were produced. A formal application for a grant of $60,000 was processed by the Audiovisual Department of the Navy on behalf of the National Resuscitation Society and presented to the National Institutes of Health. This application was for a 40-minute film and the free distribution of copies to all medical and dental schools. The application was considered by the Council for Neurological Diseases and Blindness which indicated that approval would be considered if $15,000 to $20,000 of the amount requested was obtained elsewhere. More than a year was expended in an effort to find such a co-sponsor. Owing to the fact that no credit line could be permitted any industrial group for such a contribution, the Government's offer could not be realized.

## Conclusions

In spite of the fact that long range indoctrination has met so many obstacles, the problem of hypoxia looms as large and is as acute as ever. The first step in its solution is undoubtedly the preparation and the wide use of a 20-minute film which will broadcast the doctrine of hypoxia. A film, while providing the basis for a long range approach in the medical and the dental school, would by no means be restricted to undergraduate groups. It would be available to all State and County Medical Societies as well as to hospital staffs. The Navy has expressed a willingness to help in distribution.

Perhaps a number of Heart Societies would be willing to assist on the assured basis of distribution and of providing the community with better protection against cardiac arrest. Which Society will be the first to appropriate a thousand dollars to activate this vital program? Will it be your Heart Society? Why not bring this up at the next meeting?


## Didactic and Clinical Course in Respirocardiac Resuscitation

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# The Query Corner

READERS are invited to submit queries on all aspects of cardiovascular diseases. Insofar as possible these will be answered in this column by competent authorities. The replies will not necessarily represent the opinions of the American College of Cardiology, the JOURNAL or any medical organization or group, unless stated. Anonymous communications and queries on postcards will not be answered. Every letter must contain the writer's name and address, but these will not be published.

## Oleomargarine Prepared from Corn Oil

*Query: Is there an oleomargarine available wholly prepared from vegetable fat sources? If so, is this margarine available in a salt free form?*

Answer: A margarine, prepared wholly from corn oil, is now available in pharmacies (Emdee Margarine, Pitman-Moore Company). It may make it easier to maintain patients on a rigid diet low in animal fat and will provide a liberal intake of unsaturated fatty acids.

As yet the preparation is not available in a salt-free form. A letter from the Research Department of the manufacturer states "for purposes of palatability, Emdee Margarine has had salt added to approximate the amount contained in butter or other salt margarines. This amounts to about 12 mg Na per gram of margarine, or about 50 mg per teaspoonful."

## Anticoagulants in Impending Infarction

*Query: Are anticoagulants of any value in impending myocardial infarction?*

Answer: This question is difficult to answer because impending myocardial infarction is a very poorly defined syndrome. Also, there have been no methods by which control studies could be made to compare the effect of treatment with and without anticoagulants in impending infarction.

The identification of this condition depends to a great degree on the premonition of the clinician. It is true that clinical experience may sensitize one to the early and accurate recognition of impending infarction but errors are bound to creep in due to the effect of heightened enthusiasm about this subject.

Dr. E. Sterling Nichol who is a recognized authority on the subject has just completed a study of 313 cases of impending infarction. This paper is in press at the present time and has not been published. He has depended on close observation of these patients and criteria which he has established. In his estimation, when treated early, only 6.7% of these 313 cases of impending infarction developed unmistakable signs of infarction or conversely he was able to avert this disaster in 92.3% of the cases.

In summary, it would seem logical that if one believed that anticoagulants are of value in an established infarction and if one has decided that such a condition is imminent, then certainly nothing can be lost and everything gained by administration of anticoagulants when an infarction is impending.

HERBERT E. EICHERT, M.D.
Miami, Florida

## Heparin vs. Dicumarol

*Query: Ignoring the factor of cost and convenience, do you consider heparin a superior anticoagulant to the oral anticoagulants like dicumarol?*

Answer: It has been generally agreed that heparin as an anticoagulant is superior to all the oral anticoagulants. The latter act by means of a toxic effect upon the liver production of prothrombin whereas heparin is a physiologic substance with a wide margin of safety. It acts very quickly and effectively, can be used during pregnancy or in the presence of a mild liver disease, has few contraindications, and is rapidly neutralized by protamine sulfate, toluidine blue, or whole blood. There is much excellent experimental evidence that it is more effective than

the prothrombin depressing drugs in the prevention of thrombosis unless the latter are given in doses large enough to lower prothrombin levels dangerously. Platelet adhesiveness, an important initiating factor in thrombosis, is promptly lowered by heparin whereas dicumarol is ineffective despite good hypoprothrombinemia. The oral anticoagulants do not prolong clotting time until adequate prothrombin depression has been present for four to seven days.

HYMAN ENGELBERG, M.D., F.A.C.C.
Beverly Hills, California

### Anticoagulants in Impending Infarction

*Query: Should anticoagulants be used routinely in treating patients with so-called impending infarction? Is heparin better than oral anticoagulants for this purpose?*

Answer: The diagnosis of impending infarction can be made with absolute certainty only in retrospect. Nevertheless, the diagnosis will be correct in many instances when patients with known coronary disease have a fairly rapid decline in their clinical picture and have evidence of increasing ischemic changes in the electrocardiogram. Heparin should be promptly given in full anticoagulant doses in these individuals. For optimal anticoagulant action a dose of 150 mg concentrated aqueous heparin (100 or 200 mg/cc) should be administered subcutaneously every 12 hours. However, a dose of 300 mg once every 24 hours is often adequate.

Heparin is better than oral anticoagulants since in addition to its prompt, efficient anticoagulant action, it results in a clearing of alimentary lipemia. It has been shown by many investigators that lipemia, apart from its contribution to the atherosclerotic process itself, has many actions. Lipemia increases coagulability of the blood, platelet adhesiveness, aggregation of erythrocytes and plasma viscosity, interferes with oxygen uptake by the tissues, decreases arterial oxygen saturation, and inhibits fibrinolysis. These harmful effects of lipemia *per se* are eliminated by the use of heparin but not by any of the oral anticoagulants which have no effect upon serum lipids, lipoproteins, or lipemia.

It is probable that its action in clearing lipemia also indicates the use of heparin as the anticoagulant of choice for the entire anticoagulant period in the therapy of acute myocardial infarction. In a recent study at the Los Angeles County General Hospital (as yet unpublished) it was found that when patients with severe risk myocardial infarction were treated with heparin alone as the anticoagulant for three to four weeks, the mortality was 25 per cent lower than in a comparable control group who received oral anticoagulants with heparin being given only for the initial two to three days.

HYMAN ENGELBERG, M.D., F.A.C.C.
Beverly Hills, California

### Hemorrhage Due to Anticoagulants

*Query: What are the present day methods for treating very prolonged prothrombin times and hemorrhage during anticoagulant therapy?*

Answer: Transfusions of whole blood and the intravenous administration of vitamin $K_1$ (Mephyton®) are used in the treatment of hemorrhage resulting from the use of prothrombin depressing drugs. Although vitamin $K_1$ is far more efficient than the previously used preparations, several hours usually elapse before elevation of the depressed prothrombin levels occurs. It should also be remembered that the action of the oral anticoagulants persists for several days after the last dose has been taken so that repeated administration of vitamin $K_1$ will probably be indicated.

HYMAN ENGELBERG, M.D., F.A.C.C.
Beverly Hills, California

# Book Reviews

**Digitalis** by E. Gray Dimond. Thomas, Springfield, Ill., 1957, pp. 255, $7.00.

This collection of twelve papers, of which nine were presented at a two-day postgraduate session devoted to the single subject of digitalis, comprehensively reviews the recent experimental studies and some of the current clinical concepts of the action and use of digitalis. The 234 pages of this volume provide the reader for the first time with a complete up-to-date story of the known facts about digitalis. The opening chapter is Ralph Major's simple and inspiring account of William Withering's life and a reprinting of Withering's "An Account of the Foxglove and Some of Its Medical Uses." Next, K. K. Chen "keynotes" some of the fields of physiologic and biochemical research dealing with the action and pharmacology of digitalis which have been most fruitful. R. J. Bing pinpoints the exact locus of action of digitalis on the contractile protein of the muscle cell during metabolic recovery rather than initially during the excitatory phase.

Using the embryonic duck heart assay method Meyer Friedman confirms experimentally that digitalis is completely absorbed from the gastrointestinal tract, that the major portion of digitalis is excreted via the urine, and that man destroys approximately 0.1 g of digitalis or 0.1 mg of digitoxin a day. Friedman further shows that there is neither selective concentration of digitalis in the heart muscle nor in the extravascular fluid. In view of the body's "minute capacity to destroy digitoxin" (0.050–0.075 mg of digitoxin per day), he points out the danger of overdosage when maintenance doses in the range of 0.2 mg of digitoxin are employed.

Through work done in Geiling's laboratory, Okita maps out the metabolic fate of radioactive digitoxin and shows that the myocardium has no preferential affinity for digitalis since the glycoside is rapidly changed to its metabolites. Grisola and Ito, from oxygen utilization studies performed on mitochondria treated with digitalis, agree with Bing and reason that the beneficial effect of digitalis is to expedite the effective utilization of high energy phosphate at the energy production or transfer level.

Luisada and Aravanis revive the claims that part of the salutary action of digitalis is to actively decrease the diastolic length of heart muscle. They point out that this effect has been overlooked or unexplained by other investigators and can be demonstrated by carefully manipulated and magnified electrograms obtained by recording the isotonic movements of the papillary muscles or ventricle strips of dogs or cats.

Batterman uses a number of graphic schematic diagrams to support certain ideas he has as to the various clinical effects obtained with digitalis. He is not in accord with some of the previous writers' beliefs and he explains the variations in the "therapeutic range" of digitalis encountered when the usual average digitalizing doses are employed as being due to the individual and his cardiac status. Using a "redigitalizing" technic on patients on maintenance therapy, Batterman shows that the digitalis effect obtained in an individual is of more important consideration than the choice of glycoside or dosage used. Sodeman offers some excellent advice on the proper bedside management of the patient on digitalis therapy.

In the final two papers Bernard Lown reviews the relationship between potassium and digitalis in the therapy of heart failure and discusses the auricular arrhythmias due to digitalis. The last chapter in this well-organized and very readable book is the verbatim report of the panel discussion following presentation of these papers.

NORMAN A. DAVID, M.D.
ISIDOR C. BRILL, M.D.

**Low-Fat Cookery.** By Evelyn S. Stead and Gloria K. Warren. McGraw-Hill, New York, 1956, pp. 184, $3.95.

This is by far the best written and most carefully prepared book on the low fat diet at levels of 25 and 50 grams each day. Considerable skill and practical experience have gone into the

problem of attractive food preparation. Specific products are mentioned by brand names and instructions as to how to prepare each dish have been written with the problems of the average housewife in mind.

No effort is made to differentiate between saturated and unsaturated fats. Because many of the favorite American foods are relatively high in saturated fat this diet tends to be somewhat low in unsaturated fat. In view of the recent research work more unsaturated fat could be added to the suggested diet very easily. The hard problem is to cut the saturated fat intake and still retain tasteful foods, a hurdle the authors have achieved very successfully.

Such degree of skill and experience is demonstrated that it would seem worthwhile for a second edition of this book to be written, this time using seafoods more frequently to which unsaturated fat may be added in preparation or as side dishes.

From ethnologic studies and knowledge of patients' dietary habits, it would seem that permitting about 14 per cent saturated fat caloric intake and building to about 25 per cent total fat caloric intake by the addition of unsaturated fats would better satisfy the American palate and yet constitute effective treatment.

AVERLY M. NELSON, M.D.

**Mechanisms of Hypertension** by Henry Alfred Schroeder, M.D. Thomas, Springfield, Illinois, 1957, pp. 379, $9.00.

For many years Dr. Schroeder has been making significant contributions to the understanding and treatment of hypertension and hypertensive diseases. In this volume he elaborates in detail his present conceptions of the mechanisms which elevate arterial pressure and maintain it at an abnormally high level. The discussion of pathogenesis is followed by a comprehensive description of Schroeder's methods of treatment of hypertensives—he was a pioneer in the simultaneous use of multiple anti-pressor agents. The book closes with chapters on the pathogenesis and treatment of atherosclerosis.

Schroeder's monograph is not intended for those with merely casual or general interest in hypertensive states. It is frankly a presentation of working hypotheses of the pathogenesis of hypertension which the author has developed after long study and research. Few if any of these hypotheses have as yet sufficient unequivocal support to elevate them to the dignity of theories. But they may help in directing future investigation.

The subject of pathogenesis is introduced by a description of four hypertensive patients in whom, respectively, an important pathogenetic factor was neurogenic vasospasm, pyelonephritis, narrowing of the mouths of the renal arteries, and an adenoma of the adrenal cortex. In this chapter the mechanisms of some of the consequences of hypertension are discussed. Schroeder favors the theory (previously advanced by another) that hyperemia rather than ischemia is the fundamental pathogenetic mechanism in hypertensive retinopathy. He believes that both azotemia and diastolic hypertension are necessary preconditions for the development of arteriolar necrosis in hypertensive disease; to the reviewer, the obligatory role of azotemia seems questionable.

An excellent brief chapter on constitutional factors is followed by detailed chapters on neurogenic and nephrogenic effector mechanism. These sections contain much original work. Schroeder now believes it possible that pherentasin, the pressor body described by him a few years ago, may be a form of hypertensin (angiotonin). The hypothesis is advanced that abnormal trace metals may produce hypertension through action on enzymatic mechanisms. In Chapter VI the possible role of trace metal in cardiovascular disease is examined in detail.

The concluding chapters on the treatment of hypertensive and atherosclerotic patients contain considerable information of practical importance which has been unveiled by Schroeder or which is not generally known. The experience of the reviewer does not accord with Schroeder's opinion that the control of hypertensive disease in man "is no more difficult, in fact much less so, than the control of diabetes mellitus."

This is a thought provoking monograph, well worthwhile for the serious student of hypertensive disease. ARTHUR M. FISHBERG, M.D.

# College News

## SEVENTH INTERIM MEETING

### AMERICAN COLLEGE OF CARDIOLOGY

**Jung Hotel, New Orleans, Louisiana**

**November 20 to 22, 1958**

## Scientific Program

### First Scientific Session

*Thursday, November 20, 1958, 1:00 to 5:00 P.M.*

PRESENTATIONS BY NEW ORLEANS GROUP

1. Heart Failure in Infancy.
   RICHARD L. FOWLER, M.D.

2. Complex Carbohydrate Substances of the Aorta and a Speculative Appraisal of Their Relationship to Disease.
   GERALD S. BERENSON, M.D.

3. The Influence of Tropical Weather on the Heart.
   GEORGE E. BURCH, M.D.

4. Hemodynamic Alterations Caused by Successful Transaortic Valvuloplasty.
   CHARLES B. MOORE, M.D.

5. Clinical Application of the Effects of Change in Cycle Length on the Rate of Repolarization in the Ventricular Myocardium and on Conductivity in the Specialized Tissues.
   MANUEL GARDBERG, M.D.

6. Myocardial Infarction in Young Adults.
   THOMAS N. JAMES, M.D. and ROBERT W. BROWN, M.D.

### Fireside Conferences

*Thursday, November 20, 1958, 8:30 to 10:00 P.M.*

1. Pericarditis.
   LOUIS F. BISHOP, M.D.
   Assistant Clinical Professor of Medicine, New York University Medical School, New York, N. Y.
   CRAWFORD W. ADAMS, M.D.
   Instructor in Clinical Medicine, Vanderbilt University Medical School, Nashville, Tenn.

2. Use of Enzymes in the Diagnosis of Heart Disease.
   CLARENCE M. AGRESS, M.D.
   Associate Clinical Professor of Medicine, University of California Medical School, Los Angeles, Calif.
   JOHN S. LADUE, M.D.
   Associate Clinical Professor of Medicine, Cornell University Medical College, New York, N. Y.

3. Collagen Disease and the Cardiovascular System.
   EDGAR HULL, M.D.
   Professor of Medicine, Louisiana State University School of Medicine, New Orleans.
   GEORGE R. MENEELY, M.D.
   Associate Professor of Medicine, Vanderbuilt University School of Medicine, Nashville, Tenn.

4. Vectorcardiography.
   MANUEL GARDBERG, M.D.
   Clinical Associate Professor of Medicine, Louisiana State University School of Medicine, New Orleans.
   SIMON DACK, M.D.
   Assistant Clinical Professor of Medicine, New York Medical College, New York, N. Y.

5. Indications for the Use of Angiocardiography and Cardiac Catheterization.
   CHARLES T. DOTTER, M.D.
   Professor of Radiology, University of Oregon Medical School, Portland, Oregon.

   RICHARD L. FOWLER, M.D.
   Professor of Pediatrics, Louisiana State University School of Medicine, New Orleans.

## Second Scientific Session

*Friday, November 21, 1958, 9:00 A.M. to Noon*

*Symposium on*
DIAGNOSIS OF ARTERIAL DISEASE

*Moderator:* GEORGE E. BURCH, M.D.
Professor and Chairman, Department of Medicine, Tulane University School of Medicine, New Orleans.

1. Pathogenesis and Natural History of Peripheral Arterial Disease.
   RUSSELL L. HOLMAN, M.D.
   Professor of Pathology, Louisiana State University School of Medicine, New Orleans.

2. Clinical Evaluation.
   RAY W. GIFFORD, JR., M.D.
   Assistant Professor of Medicine, Mayo Foundation, Rochester, Minn.

3. Evaluation of Peripheral Vascular Flow.
   GEORGE E. BURCH, M.D.
   Professor and Chairman, Department of Medicine, Tulane University School of Medicine, New Orleans.

4. Angiographic Diagnosis.
   CHARLES T. DOTTER, M.D.
   Professor of Radiology, University of Oregon Medical School, Portland, Oregon.

5. Panel Discussion.

## Third Scientific Session

*Friday, November 21, 1958, 2:00 to 5:20 P.M.*
*Symposium on*
MEDICAL TREATMENT OF ARTERIAL DISEASE

*Moderator:* EDGAR HULL, M.D.
Professor of Medicine, Louisiana State University School of Medicine, New Orleans.

1. Acute Peripheral Arterial Occlusion.
   STANFORD WESSLER, M.D.
   Assistant Professor of Medicine, Harvard Medical School, Boston, Mass.

2. Chronic Arterial Insufficiency.
   WILLIAM T. FOLEY, M.D.
   Assistant Clinical Professor of Medicine, Cornell University Medical College, New York, N. Y.

3. Cerebral Arterial Disease.
   CLARK H. MILLIKAN, M.D.
   Associate Professor of Neurology, Minnesota Graduate School, Mayo Clinic, Rochester, Minn.

4. Indications for Surgical Intervention.
   ALTON OCHSNER, JR., M.D.
   Vascular Surgeon, Oschner Clinic, New Orleans.

5. Panel Discussion.

## Fourth Scientific Session

*Saturday, November 22, 1958, 9:00 A.M. to Noon*

*Symposium on*
SURGICAL TREATMENT OF PERIPHERAL ARTERIAL DISEASE

*Moderator:* OSCAR CREECH, JR., M.D.
WM. HENDERSON, M.D.
Chairman and Professor of Department of Surgery, Tulane University School of Medicine, New Orleans.

1. Peripheral Arterial Insufficiency.
   PAUL T. DECAMP, M.D.
   Assistant Professor of Surgery, Tulane University School of Medicine, New Orleans.

2. Aorta and Large Arteries.
   DENTON A. COOLEY, M.D.
   Assistant Professor of Surgery, Baylor University, New Orleans.

3. Cerebral Aneurysms.
   RAEBURN C. LLEWELLYN, M.D.
   Assistant Professor of Surgery, Division of Neurologic Surgery, Tulane University School of Medicine, New Orleans.

4. Physiology of Arteriovenous Aneurysms.
   GEORGE C. MORRIS, JR., M.D.
   Director of Surgical Research Laboratories, Baylor University College of Medicine, New Orleans.

5. Congenital Abnormalities of the Major Cardiac Vessels.
   W. STERLING EDWARDS, M.D.
   Assistant Professor of Surgery, Medical College of Alabama, Birmingham, Ala.

6. Panel Discussion.

## Fifth Scientific Session

*Saturday, November 22, 1958, 2:00 to 5:00 P.M.*

PRESENTATION OF SCIENTIFIC PAPERS BY MEMBERS

1. Acute Benign Idiopathic or Nonspecific Pericarditis Associated with the Influenza Virus.

   CRAWFORD W. ADAMS, M.D.

   Department of Medicine, Vanderbilt University Medical School, Nashville, Tenn.

2. Auscultatory and Phonocardiographic Studies of Pure Mitral Insufficiency.

   JOSEPH K. PERLOFF, M.D.

   Department of Cardiology, Georgetown University Hospital, Washington, D. C.

3. Experimental and Clinical Dissolution of Peripheral Clots by the Fibrinolytic Agent Plasmin.

   ALVIN H. FREIMAN, M.D.

   Sloan-Kettering Division, Cornell University Medical College, New York, N. Y.

4. Cinecardioangiography; Selective Left Ventricular Opacification in Congenital Heart Disease.

   EARL K. SHIREY, M.D., *and* F. MASON SONES, JR., M.D.

   Department of Cardiovascular Diseases, Cleveland Clinic, Cleveland, Ohio.

5. Can Routine Electrocardiographic Technic Be Simplified? Suggestion of a New Method.

   ALDO JACONO, M.D., *and* ALDO A. LUISADA, M.D.

   Division of Cardiology, Chicago Medical School, Chicago, Ill.

6. Management of Thrombophlebitis with Butazolidin.

   IRWIN D. STEIN, M.D.

   Department of Medicine, Columbia University, New York, N. Y.

# General Convention Schedule

### WEDNESDAY, NOVEMBER 19, 1958

6:00 P.M.–11:00 P.M.
84th Board of Trustees Dinner Meeting
Rooms 9 and 10

### THURSDAY, NOVEMBER 20

10:00 A.M.–6:00 P.M.
Registration: Mezzanine

1:00 P.M.–5:00 P.M.
First Scientific Session, Tulane Room

6:30 P.M.–8:00 P.M.
Dinner (informal), Green Room

8:30 P.M.–10:00 P.M.
Fireside Conferences, Tulane Room

### FRIDAY, NOVEMBER 21

9:00 A.M.–5:00 P.M.
Registration: Mezzanine Lounge #1

9:00 A.M.–NOON
Second Scientific Session, Tulane Room

NOON–2:00 P.M.
Luncheon (No official commitment)

2:00 P.M.–5:20 P.M.
Third Scientific Session, Tulane Room

6:30 P.M.–7:30 P.M.
Reception and cocktails, Mezzanine Lounge #2

7:30 P.M.
Banquet (dress optional), Tulane Room

### SATURDAY, NOVEMBER 22

9:00 A.M.–5:00 P.M.
Registration: Mezzanine Lounge #1

9:00 A.M.–NOON
Fourth Scientific Session, Tulane Room

NOON–2:00 P.M.
Luncheon (No official commitment)

2:00 P.M.–5:00 P.M.
Fifth Scientific Session, Tulane Room

6:00 P.M.–10:00 P.M.
85th Board of Trustees Dinner Meeting
(Rooms 9 and 10)

## Cardiology—An Encyclopedia

Our readers have been informed (AM. J. CARDIOL. 1: 293, 1958) about the preparation of *Cardiology—An Encyclopedia of the Cardiovascular System*, sponsored by the College. This systematic treatise on the heart and vessels, edited by Dr. A. A. Luisada, with the assistance of numerous other editors, will be published by Blakiston (McGraw-Hill) of New York. The work will be in loose-leaf form and consist of the following five volumes:

Vol. I—The Normal Heart. Vol. II—Methods. Vol. III—Clinical Cardiology. Vol. IV—Clinical Cardiology. Therapy. Vol. V—Related Fields.

It is expected that the first four volumes, consisting of approximately 800 pages each, will appear simultaneously in the summer of 1959, thus providing investigators and clinicians with the most complete information about the cardiovascular system.

It is planned that the fifth volume will follow approximately a year later. Supplements and revisions will be sent every two years, thus keeping the work up-to-date in spite of the rapid evolution of our knowledge in the cardiovascular field.

Over 300 contributors from all over the world have prepared the manuscripts for this monumental work. Further details and complete listing of contents will be presented to our readers in a subsequent announcement.

A special discount will be given to Members and Fellows of the College from the list price to be announced in the Spring of 1959. Subscription cards will be sent by the Secretary of the College.

## 1959 ANNUAL MEETING

The Eighth Annual Meeting of the College will be held on May 25–29, 1959 inclusive at the Benjamin Franklin Hotel, Philadelphia. Dr. Robert P. Glover has been appointed Local Convention Chairman.

### Call for Abstracts of Papers

All members of the College are requested to submit or urge their associates to submit 250 word abstracts of original scientific studies in the field of cardiovascular diseases for the Annual Meeting of the College in Philadelphia on May 25–29, 1959. These abstracts are to be mailed to the Chairman of the Program Committee, Dr. John S. LaDue, 115 East 61st Street, New York 21, N. Y., for consideration by the Program Committee.

Eight papers will be selected for presentation by members of the College at the Annual Meeting. Abstracts must be submitted by February 15, 1959. Your cooperation is essential to our having a good meeting.

# Announcements

## Report of the Third World Congress of Cardiology

By now the 3,000 cardiologists and allied scientists who attended the Third World Congress of Cardiology in Brussels have returned to their own lands and have related their sundry travel experiences to all who would listen. This is their privilege, since, as Baron Munchausen contends, "A traveler has a right to relate and embellish his adventures as he pleases, and it is very impolite to refuse that deference and applause he deserves." We are certain that they will not abuse this right by extending it to the scientific sessions of the Congress.

For each participant the value and success of the Congress depend on the highlights, knowledge, impressions, and experiences which his trip provided. With the passage of time the minor discomforts and disappointments are happily forgotten and the benefits of the Congress manifest themselves. In a reflective, impartial spirit one can now assay the intrinsic worth of the Congress. In each instance the individual factors vary, but we believe none will seriously question the benefits of the meeting and the educational merits of the travels associated with it. We hope, like Samuel Johnson, "that the mind was enlarged by it, and that an acquisition of dignity of character was derived by it."

Five volumes distributed to the registrants record the program, grand conferences, general conferences, symposia, and communications, and delineate the giant scope of the Congress. The Congress committee is to be complimented on this heroic endeavor to present and integrate this truly mountainous amount of data. These volumes are an index of the fertile state of cardiologic research throughout the world. Their contents must be chewed and digested with diligence and attention, since they provide the essence of the latest scientific thought and knowledge. For several years to come they will remain a useful guide to current worldwide research in cardiology.

Although the excellent contributions are too numerous to mention individually, any report on the Congress must include the thoughtful and stimulating address by Dr. Ignacio Chávez of Mexico, the new president of the next World Congress and an outstanding member and vice-president of The American College of Cardiology, on "Grandeur and Poverty of Medical Specialization—Aspiration Toward a New Humanism." Discussing one of the most crucial problems of our time, Dr. Chávez analyzed the profound scientific and technical transformation of medicine which has resulted in the preeminence of specialization, fertile in valuable achievements but also pregnant with risk. According to him, "Specialization carries within itself an enormous expansive force of progress, but also contains the germ of regression in the intellectual and spiritual realm. Specialization means fragmentation, partial vision and limitation of our horizon. What is gained in depth is lost in breadth. To master one field of knowledge one must abandon the rest; man thus confines himself to one point and sacrifices the whole vision of science and the universal vision of his world. . . . His general culture suffers, then his scientific training suffers, for he ceases to look on science as a whole in order to keep a poor little portion in his hands; finally his moral world suffers, for the sacrifice of culture constitutes a sacrifice of values which should set the standards of his life. In this drama of the present-day scientist an imminent risk is foreshadowed—the dehumanization of medicine and the dehumanization of the physician. . . . He must react against the tendency observed in younger generations to consider only laboratory investigation scientific, and to look with disdain on clinical research. Scientific quality does not depend on the tools that are used, but rather on the method which is followed; merit rests on the creative idea."

Dr. Chávez emphasized, "You cannot be specialists in cardiology if you are not at the same time clinicians and scientists. The true specialists are those who can advance the knowledge in their field." For the specialist of today Dr. Chávez prescribed as a complement to scientific education a humanism which should include the knowledge of languages and history, frequent contact with the modern classics, and the love of beauty, music, and plastic arts. "Such humanism projected into science invites man to flee from selfish isolation and impels him to work nobly in collaboration and counteracts the harmful tendencies that arise from specialization. . . . You cannot be good cardiologists as long as you are not cultured men."

Equally important to cardiologic knowledge and general culture as the formal presentations were the numerous occasions for informal discussions with scientists from all over the world. These chance encounters exposed favorite ideas to critical scrutiny and often produced a new point of view and a better informed opinion. Greater understanding of mutual problems, not only medical, but social, economic, and political ones as well, was frequently a spontaneous outgrowth of such talks. This Congress presented the opportunity of re-examining fixed thought habits and encouraged a quality which Thouless describes as "flexibility of mind," an ability to try out new ways of thinking and to make unfamiliar assumptions. The development of this type of mind will do much to ease international tensions and enhance the geometric expansion of cardiologic research and knowledge.

Many members of The American College of Cardiology participated in the sessions of the Congress. With such extensive representation one cannot help wondering why delegates of The American College of Cardiology were not officially included in the organization of the Congress. This situation should certainly be corrected in the next World Congress in Mexico.

Great interest in THE AMERICAN JOURNAL OF CARDIOLOGY was displayed by the Congress members with whom we discussed the Journal. They felt that the Journal, with its accent on clinical cardiology and humanism (as defined by Dr. Chávez), meets the need for accurate information and the greater "flexibility of mind" so necessary for real progress in all science. From these discussions it was obvious that the Journal has attained international stature and value.

Almost needless to say, the various receptions at the Hotel de Ville, the social and musical events, and the International Exposition rounded out a very active week for the Congress members and their wives.

RAYMOND HARRIS, M.D., F.A.C.C.
*Assistant Editor*

**Symposium on Congenital Heart Disease**

A Symposium on Congenital Heart Disease will be held December 29 and 30, 1958, in Washington, D. C., sponsored by the Section of Medicine, American Association for the Advancement of Science, and endorsed by the American Heart Association and the American College of Cardiology.

The Symposium will be comprised of four sessions of several papers each: I, Development of the Heart and Origins of Congenital Heart Disease; II, Pathologic Physiology; III, Diagnosis; and IV, Surgical Therapy.

The complete program will appear in the December issue of this Journal.